MAY 14 1924

VOLUME 27 NUMBER 5

AMERICAN JOURNAL

OF

DISEASES OF CHILDREN

EDITORIAL BOARD

CLIFFORD G. GRULEE, Chicago

OSCAR M. SCHLOSS, New York City — W. McKIM MARRIOTT, St. Louis

FRITZ B. TALBOT, Boston — JOHN HOWLAND, Baltimore

H. F. HELMHOLZ, Rochester, Minn.

MAY, 1924

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $4.00

Entered as Second-Class Matter, January 4, 1911, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

CONTENTS OF PREVIOUS NUMBERS

FEBRUARY, 1924. NUMBER 2

Extinction Tests in Scarlet Fever. John A. Toomey, M.D., and John D. Nourse, M.D., Cleveland.

Enterolith as Cause of Chronic Obstipation in a Breast-Fed Infant. Edwin Lee Miller, M.D., and Frank C. Neff, M.D., Kansas City, Mo.

Report of a Case of Healed Miliary Tuberculosis. Ridgely W. Baer, M.D., Frederick, Md.

Tuberculosis of the Tonsils and Adenoids: A Clinical and Roentgen-Ray Study of Fifty Cases Observed for Five Years After Operation. P. B. MacCready, M.D., and S. J. Crowe, M.D., Baltimore.

Blindness and Other Diseases in Children Arising from Deficient Nutrition (Lack of Fat-Soluble a Factor). C. P. Bloch, M.D., Copenhagen, Denmark.

A Clinical Study of Rickets in the Breast-Fed Infant. L. R. DeBuys, M.D., New Orleans.

Review of the Literature for 1921 and 1922 on Neurology of Children. August Strauch, M.D., Chicago.

Acute Hemorrhagic Pancreatitis Resulting from Round-Worms. Report of Case. W. E. Gallie, M.D., and Alan Brown, M.D., Toronto.

MARCH, 1924. NUMBER 3

Frontispiece.

Obituary. Dr. L. Emmett Holt.

Atonic Insufficiency of the Stomach a Cause of Vomiting and of Lack of Appetite in Infants. Gustaf L. Lindberg, M.D., Norrköping, Sweden.

Genito-Suprarenal Syndrome (Suprarenal Virilism) in a Girl One and a Half Years Old, with Successful Operation. Arthur Collett, M.D., Christiana, Norway.

The Teeth in Childhood. Donald C. Mebane, M.D., Rochester, Minn.

Two Cases of Acute Epidemic Encephalitis Occurring in One Family. Franklin G. Ebaugh, M.D., Philadelphia.

Kidney Diseases in Infants and Children. II. Malignant Hypertension Nephritis: Primary Sclerotic Kidney (Schrumpfniere). Herman Schwarz, M.D., New York.

Studies in the Uric Acid Metabolism of Children. Jerome S. Leopold, M.D.; Adolph Bernhard, M.A., and Harry G. Jacobi, M.D., New York.

Measles Transmitted by Blood Transfusion: Report of a Case. Harry Baugness, M.D., Minneapolis.

Recent Work in Anatomy, Physiology and Pathology of Infancy and Childhood. James B. Holmes, M.D., Baltimore.

Book Review.

APRIL, 1924. NUMBER 4

Studies on Anemia in Infancy: The Urobilin Content of the Stools of Normal Infants. B. S. Denzer, M.D., and K. K. Merritt, M.D., New York.

Meningeal Hemorrhages in the New-Born and Their Remote Consequences. Alfred Gordon, M.D., Philadelphia.

Studies on the Acidity (Hydrogen-Ion Concentration) of Infants' Stools. Frederick F. Tisdall, M.D. (Tor.), and Alan Brown, M.B. (Tor.), Toronto.

Thrombocytopenic Purpura Hemorrhagica Successfully Treated by Splenectomy. Murray H. Bass, M.D., and Philip Cohen, M.D., New York.

Anemia in the New-Born. Harry H. Donnally, M.D., Washington, D. C.

Acute Pelvic Abscess in Children. Philip Rosenblum, M.D., and Ralph B. Bettman, M.D., Chicago.

The Estimation of the Volume of Blood in Normal Infants and in Infants with Severe Malnutrition. Harry Bakwin, M.D., and Helen Rivkin, M.A., New York.

A Comparison of the Metabolism of Some Mineral Constituents of Cow's Milk and of Breast Milk in the Same Infant. Chi Che Wang, Ph.D.; David B. Witt, M.D., and Augusta R. Felcher, A.B., Chicago.

Acute Fatty Enlargement of the Liver in Infants. Jerome L. Kohn, M.D., New York.

Résumé of the Literature for 1921 on Tuberculosis in Childhood. M. G. Peterman, M.D., Rochester, Minn.

COPYRIGHT, 1924, BY THE AMERICAN MEDICAL ASSOCIATION

American Journal of Diseases of Children

VOL. 27 MAY, 1924 NO. 5

THE PRODUCTION OF PURULENT MENINGITIS IN THE RABBIT AND THE CHANGES IN ITS CEREBROSPINAL FLUID*

MICHIO KASAHARA
KYOTO, JAPAN

Purulent meningitis in animals has been studied in recent years by many observers, among whom may be mentioned Ritchie,[1] Wollstein,[2] M'Donald,[3] Councilman, Mallory and Wright,[4] Von Lingelsheim,[5] and Flexner.[6]

Ritchie produced purulent meningitis in the monkey by the intraspinal injection of *B. influenzae*. Similar results have been described by Wollstein. Councilman, Mallory and Wright succeeded in producing meningitis in the goat by the injection of the meningococcus into the spinal canal. Von Lingelsheim introduced the meningococcus intraspinally into two monkeys. The animals developed rigidity of the neck and of the dorsal muscles, and had a violent attack of vomiting. Similar results have been obtained by Flexner and M'Donald; other observers have, however, obtained negative results.

In the first paper I stated that the injection of virulent tubercle bacilli into the subarachnoid space of rabbits causes tuberculous meningitis, characterized by an incubation period of from five to fifteen days, followed by a period of cerebral symptoms ending almost invariably in death.

The object of this investigation is to study the changes in the spinal fluid of the rabbit in which purulent meningitis, due to pyogenic organ-

* Received for publication, Dec. 17, 1923.

* From the Department of Pediatrics of the Medical College, the Kyoto Imperial University.

1. Ritchie, J.: J. Path. & Bacteriol. **14**:615, 1910.
2. Wollstein: J. Exper. Med. **14**:73, 1913.
3. M'Donald, S.: J. Path. & Bacteriol. **12**:442, 1908.
4. Councilman, Mallory and Wright: Report of State Board of Health, Boston, 1898.
5. Von Lingelsheim: Deutsch. med. Wchnschr. **31**:1217, 1905.
6. Flexner, S.: J. Exper. Med. **9**:142, 1907.

isms, has been produced experimentally. Adult rabbits were used in all the experiments. The micro-organisms which we employed for these experiments were pneumococcus, *B. coli, B. influenzae, B. pyocyaneus,* streptococci and staphylococci.

The inoculation materials were emulsified in 0.65 per cent. salt solution. The inoculation was made by an intraspinal injection. It was effected through the posterior occipito-atloid ligament. The quantity of bacterial suspension varied from 0.25 to 0.3 c.c. The spinal fluid was withdrawn to an extent somewhat larger than the amount of suspension to be injected. The injection was made extremely slowly.

Without entering on the details of the experiments, I may make the following general statement: The inoculation of the before mentioned pyogenic organisms into the subdural space of the rabbit produces a disease characterized by a latent period of from several hours to three days, depending on the dosage and virulence of the injected organisms, followed by a period of ataxia and paralysis. From the time of the appearance of the first symptom, the severity rapidly increases and death occurs in from two to five days or somewhat later. The cerebrospinal fluid is, without exception, opaque or purulent, containing numerous polymorphonuclear leukocytes. It sometimes deposits purulent sediment. The organisms are present and demonstrable by culture and by film preparation. By necropsy it may be ascertained that certain changes are common to all the forms of meningitis. It shows purulent leptomeningitis, both on the surface of the brain and within the sulci, as well as over the spinal cord. Microscopically, it shows an extensive exudation in the pia. This consists chiefly of polymorphonuclear leukocytes. In some cases hemorrhages are found in the meninges.

There is no visible change in the abdominal and thoracic viscera. We have examined the cerebrospinal fluid at varying periods after the intraspinal inoculation with the before mentioned pyogenic organisms.

EXPERIMENT WITH PNEUMOCOCCI

The rabbits are inoculated intraspinally with 0.3 c.c. of suspension of the pneumococci. One culture on blood agar is suspended in 4 c.c. of 0.65 per cent. saline solution. A few hours after inoculation the first cerebral symptom begins. Definite paralysis occurs on the second or third day. Death occurs from the third to the fifth day. Necropsy shows fibrinous inflammatory exudation in the pia, attended by hyperemia, infiltration with polymorphonuclear leukocytes. No gross changes are visible in other organs. The results are shown in Table 1.

TABLE 1.—*Experiments with Pneumococci*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm. Polymorphonuclear	Cells per C. Mm. Lymphocyte	Remarks
1	1st	Cloudy turbid	+	0.033	0.034	+	240	46	Leptomeningitis
2	2d	Turbid	Gelatinous character	0.060	0.025	++	350	20	Leptomeningitis
3	4th	Cloudy turbid	Gelatinous character	0.060	0.031	++	950	53	Leptomeningitis
4	5th	Turbid	+	0.096	0.034	++	1,099	103	Leptomeningitis
5	5th	Cloudy turbid	Gelatinous character	0.126	0.02	++	1,238	93	Leptomeningitis

EXPERIMENT WITH COLON BACILLI

The rabbits are inoculated intraspinally with 0.3 c.c. of suspension of colon bacilli. It was isolated from the stool of an infant suffering from acute enteritis. (The subcutaneous injection with 0.1 mg. of the culture causes a small pustule to form in a mouse after twenty-four hours.) The first cerebral symptom begins two or three hours after inoculation and death occurs within a few days. Necropsy shows that the pia is hyperemic. Opacity and thickening of the membrane are seen. Microscopical examination shows an exudate of abundant leukocytes. No gross changes are seen in other organs. The results are shown in Table 2.

TABLE 2.—*Experiments with Colon Bacilli*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm. Polymorphonuclear	Cells per C. Mm. Lymphocyte	Remarks
1	1st	Cloudy turbid	+	0.105	0.025	++	2,860	510	Leptomeningitis
2	1st	Turbid	+	0.264	0.019	++	2,960	81	Leptomeningitis
3	2d	Cloudy turbid	+	0.305	0.028	++	3,058	196	Leptomeningitis
4	2d	Cloudy turbid	Gelatinous character	0.26	0.009	++	2,861	103	Leptomeningitis
5	2d	Turbid	Gelatinous character	0.196	0.01	++	3,412	201	Leptomeningitis

EXPERIMENT WITH B. PYOCYANEUS

The rabbits are inoculated intraspinally with 0.3 c.c. of suspension of *B. pyocyaneus.* (The intradermal inoculation with 0.1 c.c. of this suspension causes an abscess of 6 mm. in size to form in a guinea-pig after twenty-four hours.) After intraspinal injection, a disease is developed in the animal, characterized by a latent period of from four to five hours, followed by a period of cerebral symptoms that terminates in death within three days. On necropsy, the meninges of the brain and spinal cord are seen to be inflamed and often covered with a

purulent exudation, which is most marked at the convexity of the brain. No visible changes are seen in the abdominal and thoracic viscera. The results are given in Table 3.

TABLE 3.—*Experiments with B. Pyocyaneus*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Turbid	+	0.048	0.031	++	2,860	280	Leptomeningitis
2	2d	Cloudy turbid	+	0.024	0.026	+	680	171	Leptomeningitis
3	2d	Turbid	+	0.056	0.035	++	563	240	Leptomeningitis
4	2d	Cloudy turbid	+	0.096	0.019	++	1,238	192	Leptomeningitis
5	3d	Turbid	+	0.16	0.034	+	907	121	Leptomeningitis
6	3d	Cloudy turbid	+	0.098	0.038	+	708	201	Leptomeningitis

EXPERIMENT WITH STREPTOCOCCI

Rabbits are inoculated intraspinally with 0.3 c.c. of suspension of streptococci. (The intradermal inoculation with 0.1 c.c. of this suspension causes a local abscess of 5 mm. in size to form in a rabbit after twenty-four hours.) The animal in the incubation period of from two to three days is apparently normal. Definite paralysis occurs on the fourth day. The disease terminates in death. The pia mater is everywhere congested and appears hazy and opaque. A fibrinous inflammatory exudation is seen in the meninges. This consists chiefly of polymorphonuclear leukocytes. The abdominal and thoracic viscera are negative. The results are shown in Table 4.

TABLE 4.—*Experiments with Streptococci*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Turbid	+	0.13	0.022	+	1,034	204	Leptomeningitis
2	1st	Cloudy turbid	+	0.086	0.009	+	2,085	455	Leptomeningitis
3	2d	Turbid	+	0.26	0.03	+	963	204	Leptomeningitis
4	2d	Turbid	++	0.18	0.032	++	1,077	104	Leptomeningitis
5	2d	Cloudy turbid	+	0.09	0.01	++	2,060	107	Leptomeningitis
6	3d	Turbid	+	0.13	0.009	+	1,963	203	Leptomeningitis
7	4th	Cloudy turbid	+	0.10	0.022	+	673	209	Leptomeningitis
8	6th	Turbid	+	0.09	0.020	+	870	120	Leptomeningitis

EXPERIMENT WITH STAPHYLOCOCCUS AUREUS

Rabbits are injected intraspinally with 0.3 c.c. of suspension of *Staphylococcus aureus.* (The intradermal inoculation with 0.1 c.c. of this suspension causes a pustule 3 mm. in size to form in a rabbit

after twenty-four hours.) A few hours after the intraspinal inoculation the animal becomes ataxic. On the second day paralysis of the legs occurs. Death is on the fourth or fifth day. Necropsy shows traces of fibrinous exudate over the whole base, and extending upward on the convex surface of the brain and the cerebellum. Frequently the posterior half of the brain is covered with a thick layer of pus. There are no visible changes in other organs. The results are given in Table 5.

TABLE 5.—*Experiments with Staphylococcus aureus*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Turbid	+	0.123	0.041	++	1,036	441	Leptomeningitis
2	2d	Cloudy turbid	+	0.095	0.035	++	1,024	768	Leptomeningitis
3	4th	Cloudy turbid	Gelatinous character	0.230	0.03	++	1,930	410	Leptomeningitis
4	4th	Cloudy turbid	+	0.123	0.026	++	1,980	120	Leptomeningitis

EXPERIMENT WITH STAPHYLOCOCCUS ALBUS

Rabbits are inoculated intraspinally with 0.3 c.c. of suspension of *Staphylococcus albus*. (The intradermal injection with 0.1 c.c. of this suspension causes an abscess 2 mm. in diameter to form in a rabbit after twenty-four hours.) A few hours later, the animal becomes excitable, ataxic, and paralytic. Death occurs within a few days. On necropsy it is found that there are extreme congestion, thickening and matting of the pia mater. There is no gross change in the other organs. The results are given in Table 6.

TABLE 6.—*Experiments with Staphylococcus albus*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Turbid	+	0.065	0.048	++	245	50	Leptomeningitis
2	1st	Turbid	+	0.09	0.031	++	1,510	30	Leptomeningitis
3	1st	Cloudy turbid	+	0.07	0.028	+	690	104	Leptomeningitis
4	2d	Cloudy turbid	+	0.15	0.041	+	320	60	Leptomeningitis
5	2d	Turbid	Gelatinous character	0.21	0.023	++	1,030	168	Leptomeningitis

EXPERIMENT WITH STAPHYLOCOCCUS CITREUS

Rabbits are inoculated with 0.3 c.c. of suspension of *Staphylococcus citreus*. (The intradermal injection with 0.1 c.c. of this suspension causes a small nodule with a central pustule to form in a rabbit after twenty-four hours.) Ataxia occurs on the first or the second day. Definite paralysis is seen on the third day. Necropsy reveals similar

phenomena to those of pyogenic meningitis due to *Staphylococcus aureus*. The results are given in Table 7.

TABLE 7.—*Experiments with Staphylococcus citreus*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Cloudy turbid	Gelatinous character	0.16	0.034	++	1,088	203	Leptomeningitis
2	1st	Cloudy turbid	+	0.23	0.025	++	2,099	254	Leptomeningitis
3	2d	Turbid	+	0.096	0.021	++	1,088	310	Leptomeningitis
4	3d	Cloudy turbid	+	0.037	0.034	++	2,034	105	Leptomeningitis
5	3d	Turbid	Gelatinous character	0.19	0.031	++	899	231	Leptomeningitis
6	4th	Turbid	Gelatinous character	0.20	0.025	++	1,238	209	Leptomeningitis

EXPERIMENT WITH B. INFLUENZAE

Rabbits are inoculated intraspinally with 0.3 c.c. of suspension of *B. influenzae*. One culture on blood agar is suspended in 6.0 c.c. of 0.65 per cent. sodium chlorid solution. After a few hours, cerebral symptoms begin, which, in a few days, terminate in death. On necropsy the pia mater of the brain and the spinal cord are found intensely hyperemic, this being most marked at the convexity of the brain and the spinal cord. Microscopic changes in the pia mater are attended by hyperemia, and infiltration with leukocytes. Hemorrhages are found in the meninges. The results are shown in Table 8.

TABLE 8.—*Experiments with B. Influenzae*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Cloudy turbid	Gelatinous character	0.16	0.021	++	2,038	108	Leptomeningitis
2	1st	Cloudy turbid	+	0.23	0.034	++	1,039	201	Leptomeningitis
3	1st	Turbid	+	0.16	0.041	++	2,000	103	Leptomeningitis
4	2d	Turbid	+	0.09	0.026	+	1,238	86	Leptomeningitis
5	2d	Cloudy turbid	+	0.34	0.031	++	893	69	Leptomeningitis
6	3d	Turbid	+	0.21	0.028	++	2,136	263	Leptomeningitis

As these tables show, the cerebrospinal fluid of the rabbit, in which purulent meningitis due to pyogenic organisms has been produced experimentally, is opaque or purulent and shows an increase in the amount of albumin and globulin. The sugar content rapidly decreases. It shows a great predominance of polymorphonuclear cells. It may contain actual fragments of purulent material, which soon sink to the bottom. A marked clot formation of gelatinous character is always present.

SUMMARY

Subdural inoculation of virulent pyogenic organisms (pneumococci, *B. coli, B. influenzae, B. pyocyaneus,* streptococci and staphylococci) by an atlanto-occipital injection causes purulent meningitis in rabbits. The picture of the spinal fluid of the infected rabbit closely resembles that of purulent meningitis in human beings.

THE PRODUCTION OF TUBERCULOUS MENINGITIS IN THE RABBIT AND THE CHANGES IN ITS CEREBROSPINAL FLUID*

MICHIO KASAHARA
KYOTO, JAPAN

Experimental meningitis, especially tuberculous meningitis in animals, has attracted little attention in the field of medicine. The first work on the subject was that done by Manwaring [1] in 1915. He succeeded in producing in dogs and in monkeys infection of the meninges, by injecting suspensions of tubercle bacilli into the subdural space through a trephine opening in the cranium. With this exception, we have been able to find no instance of tuberculous meningitis experimentally produced.

The work embodied in this paper is part of the study of experimental meningeal infection in the rabbit.

The experiments were made on adult rabbits and consisted, first, in producing tuberculous infection of the meninges, and second, in confirming the peculiar changes in the cerebrospinal fluid.

THE NORMAL CEREBROSPINAL FLUID OF THE RABBIT

Except in monkeys and in human beings, lumbar puncture is almost impossible in animals. In order to secure the cerebrospinal fluid from the subarachnoid space of the rabbit, a puncture needle is introduced into the space between the atlas and the posterior occipital tuberosity. The skin should previously be cleansed. The needle is introduced in the median line in a slightly upward direction. After passing through the rather tough intervening tissue, the sudden cessation of resistance announces the entrance of the point of the needle into the subcerebellar cisterna and then the spinal fluid is allowed to escape, or is drawn off, slowly but continuously, to the amount, as a rule, of 1 c.c. With a little practice, the atlanto-occipital puncture in the rabbit is easily and successfully made in every case.

By the above mentioned technic we have examined the normal fluid of about thirty rabbits. The results are briefly summarized as follows:

The normal cerebrospinal fluid of the rabbit is a perfectly clear and colorless liquid of low specific gravity, usually about 1.005; its reaction is faintly alkaline. Albumin is present in a very small amount, averaging

* Received for publication, Dec. 20, 1923.

* From the Department of Pediatrics of the Medical College, the Kyoto Imperial University.

1. Manwaring, W. H.: J. Exper. Med. **15**:1, 1915.

about 0.015 to 0.019 per cent. Globulin is normally absent. The average amount of sugar is 0.054 per cent. (after the microdetermination method of Bang). The cellular constituents are extremely scanty, averaging from about zero to ten cells per cubic millimeter and consist of lymphocytes. Polymorphonuclear cells are absent. If the fluid is allowed to stand, clot formation is not seen. The total amount present is generally about from 1.5 to 2.0 c.c.

EXPERIMENTAL TUBERCULOUS MENINGITIS IN THE RABBIT

To produce tuberculous meningitis in the rabbit, we introduced the suspension of tubercle bacilli into the subarachnoid space by the atlanto-occipital injection. The cerebrospinal fluid was withdrawn usually to an extent somewhat larger than the amount of suspension to be injected. Several strains of tubercle bacilli of the human, bovine, or avian types were employed. The inoculation material was prepared by diluting emulsions of the cultures, with 0.65 per cent. saline solution, which produced the desired turbidity. The amount of suspension usually injection varied from 0.25 to 0.3 c.c. The rabbit did not develop any visible reaction in all instances after the injection of the suspension.

The inoculation of virulent tubercle bacilli into the subarahnoid space of the rabbit by the above mentioned technic, produces a disease characterized by an incubation period of from six to fifteen days, followed by a period of cerebral symptoms that terminate in death.

The symptoms and the course of the disease in the rabbit are as follows:

The animal in the incubation period is apparently normal. Head tremor, rigidity of the neck and the back muscles, head retraction, ataxia, and the convulsion and paralysis of legs characterize the period of cerebral symptoms. The animal gradually becomes emaciated and finally collapses.

The most striking meningeal changes revealed by necropsy are miliary tubercles and inflammatory exudate. The tubercles are found chiefly at the base of the cerebrum and cerebellum; somewhat less frequently and less numerous on the convexity and on the spinal cord. The pia mater was congested everywhere, and appeared hazy and opaque. The other organs of the body show no characteristic change.

The symptoms and the clinical course depend on the dosage and virulence of the cultures injected. With a very virulent culture, death occurs rapidly. With less virulent cultures, the course of the disease is prolonged.

All the experiments were repeated with nearly uniform results. The following examples, selected from many experiments, will serve for demonstration purposes.

EXPERIMENT WITH HUMAN TUBERCLE BACILLI

RABBIT 1.—Weight 2,150 gm. was inoculated with 0.3 c.c. of suspension of human tubercle bacilli. (The intradermal inoculation of 0.1 c.c. of this suspension caused a small indurated nodule to form in a guinea-pig after five days, which later softened and then formed an abscess; this abscess opened externally leaving an ulcer.) The animal showed an incubation period of ten days; the cerebral symptoms, such as head tremor, head retraction and ataxia, began on the tenth day; definite paralysis on the twenty-fifth day; with death on the thirtieth day.

Necropsy showed numerous miliary tubercles in the entire meninges. The tuberculous nodules were more extensive in the region of the blood vessels and about the cranial nerves at the base. Microscopic examination of the pia showed marked tuberculous lesions. Abdominal and thoracic viscera were negative.

EXPERIMENT WITH BOVINE TUBERCLE BACILLI

RABBIT 2.—Weight 2,000 gm., was inoculated with 0.3 c.c. of suspension of bovine tubercle bacilli. (The intradermal inoculation of 0.1 c.c. of this suspension caused a small indurated nodule to form in a guinea-pig after three days, which became an abscess after seven days.) After seven days the rabbit became excitable, after ten days, ataxic and on the fifteenth day paralysis of the legs occurred. The animal succumbed on the twentieth day after inoculation.

Macroscopically, necropsy showed numerous miliary tubercles in the meninges, especially at the base of the brain. Microscopic lesions of the pia were found in the brain and cord. There was no visible change in the viscera.

EXPERIMENT WITH AVIAN TUBERCLE BACILLI

RABBIT 3.—Weight, 2,300 gm., was inoculated with 0.3 c.c. of suspension of avian tubercle bacilli. (Three milligrams of avian tubercle bacilli were emulsified in 3 c.c. of 0.6 per cent. sodium chlorid solution.) After six days the animal showed head retraction, and on the tenth day ataxia and paralysis. Death occurred in collapse on the fifteenth day. Miliary tubercles were seen in the meninges, the phenomenon being most marked at the base of the brain. There were no gross changes in the other organs.

THE CHANGE IN THE CEREBROSPINAL FLUID IN TUBERCULOUS MENINGITIS IN THE RABBIT

At a varying period after the intradural inoculation with tubercle bacilli, we have examined the cerebrospinal fluid in rabbits. In the examination of the cerebrospinal fluid, attention was paid to the estimation of the amount of albumin, globulin and sugar, the number of cells per cubic millimeter, the type of cells present, and the clot formation. Sugar was estimated by the microdetermination method of Bang, and globulin was tested by the butyric acid method of Noguchi, and the relative strength of the reaction noted. The results are recorded in Tables 1, 2 and 3.

As these tables show, the changes in the cerebrospinal fluid in tuberculous meningitis in the rabbit are peculiar to this disease. The fluid is more or less turbid and increases in the amount of albumin and globulin. The sugar content always decreases. In the early stage of the disease, the white cells increase in number, but lymphocytes are

TABLE 1.—*Experiments with Human Tubercle Bacilli*

Rabbit	Day of Disease	Appearance	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Clot Formation
						Polymorphonuclear	Lymphocyte	
1	5th	Turbid	0.795	0.042	+	409	680	+
2	7th	Cloudy turbid	0.820	0.046	+	86	563	+
3	7th	Turbid	0.53	0.039	++	123	385	+
4	10th	Cloudy turbid	0.29	0.035	+	0	708	Gelatinous character
5	13th	Cloudy turbid	0.82	0.02	++	0	962	Gelatinous character
6	15th	Turbid	0.13	0.031	++	0	1,085	Gelatinous character
7	20th	Cloudy turbid	0.83	0.01	++	0	960	+
8	16th	Turbid	0.036	0.005	++	0	1,204	+
9	16th	Cloudy turbid	0.039	0.003	++	0	765	Gelatinous character
10	20th	Cloudy turbid	0.042	0.001	++	0	1,060	+
11	31st	Cloudy turbid	0.12	0.01	+	0	618	+
12	35th	Cloudy turbid	0.18	0.035	++	0	971	Gelatinous character
13	35th	Turbid	0.15	0.033	++	0	550	Gelatinous character

TABLE 2.—*Experiments with Bovine Tubercle Bacilli*

Rabbit	Day of Disease	Appearance	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Clot Formation
						Polymorphonuclear	Lymphocyte	
1	4th	Slightly turbid	0.025	0.05	+	8	93	—
2	4th	Turbid	0.035	0.045	+	36	103	—
3	7th	Turbid	0.041	0.039	+	4	204	—
4	15th	Cloudy turbid	0.069	0.026	+	0	736	+
5	15th	Cloudy turbid	0.078	0.032	+	0	1,090	Gelatinous character
6	20th	Cloudy turbid	0.056	0.03	+	0	132	Gelatinous character
7	25th	Cloudy turbid	0.073	0.01	+	0	693	+
8	28th	Cloudy turbid	0.125	0.031	+	9	1,056	+

TABLE 3.—*Experiments with Avian Tubercle Bacilli*

Rabbit	Day of Disease	Appearance	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Clot Formation
						Polymorphonuclear	Lymphocyte	
1	4th	Slightly turbid	0.064	0.035	+	210	280	+
2	4th	Slightly turbid	0.024	0.045	+	28	180	+
3	7th	Turbid	0.05	0.04	+	130	200	+
4	7th	Turbid	0.062	0.032	+	80	320	+
5	11th	Turbid	0.051	0.04	+	2	350	+
6	15th	Cloudy turbid	0.086	0.039	+	0	680	+
7	15th	Cloudy turbid	0.12	0.023	+	0	1,073	+
8	18th	Turbid	0.16	0.031	+	0	679	+
9	20th	Turbid	0.096	0.03	+	0	1,079	+

still predominant. Polymorphonuclear leukocytes decrease, and gradually the percentage of lymphocytes increases. In the later period the type of cells present in the fluid is always mononuclear. Clot formation is present. Sometimes it shows a marked gelatinous character.

The picture closely resembles that of tuberculous meningitis in human cases.

SUMMARY

Subdural inoculation of tubercle bacilli by atlanto-occipital injection produces in the rabbit tuberculous meningitis, followed by paralysis and death. The changes in the cerebrospinal fluid are peculiar. There is an alteration in the chemical and cellular constituents.

UROBILIN EXCRETION IN THE ANEMIAS OF INFANTS AND CHILDREN *

MURRAY H. BASS, M.D.; BERNARD S. DENZER, M.D.,
AND
HAROLD HERMAN, M.D.
NEW YORK

It is now well established that the amount of urobilin and urobilinogen in the stools is a rough index of the amount of blood destruction going on in the body. Since no large number of cases of anemia in children has been studied as regards their urobilin excretion, it seemed worth while to undertake such a study. Our plan was to determine, if possible, whether certain of the forms of anemia met with in childhood might be differentiated from others by their pathogenesis. In other words, are there some forms of anemia in infancy characterized by excessive blood destruction? It is well known that in the anemia seen in cases of hemolytic icterus, there is excessive blood destruction, evidenced by an unusually large amount of urobilin in the stools and urine. Hemolytic icterus is the best example of an anemia due to blood destruction and it seemed likely that other forms of anemia might perhaps be due to a similar process. Moreover, we felt that in studying the pathogenesis of infant anemias we might possibly be able to throw a little more light on their classification. Merely clinical classifications of anemia in childhood are very unsatisfactory, and much might be gained if we knew more about the exact process by which the anemia is brought about.

It was especially in the group of anemias known as "alimentary" that we hoped to get some positive results. It may be well to recapitulate briefly the present ideas concerning this group of cases. The fact that certain infants developed anemia when fed a diet consisting almost exclusively of milk, led Czerny and his school to make a separate group in the anemias entitled "Alimentary anemia." For a time it seemed to be proved that the diet alone was responsible for the change in the blood. However, many children were observed who, fed on the same one sided diet, failed to become anemic. Controversy therefore exists chiefly in regard to the question as to whether food alone can produce this type of anemia. Kleinschmidt believes that "A certain congenital disposition" must be associated with inadequate diet and that more than one type of faulty diet may be responsible for the anemia. French authors also found anemia occurring frequently in twins, and in prema-

* Received for publication, Jan. 21, 1924.
* From the pediatric service of Mount Sinai Hospital.

ture and debilitated infants. The blood picture in these cases is similar to that found in chlorosis of adults, a greater decrease in the percentage of hemoglobin than in the number of red cells, and for this the term "Anémie, a type chlorotique" was proposed. This classification refers merely to the morphology of the blood and suggests nothing in regard to etiology.

On the other hand, Czerny and his followers laid the blame for this alimentary anemia not only on the food, but on a particular kind of food, namely fat. They believed that an excess of milk fat in infants' diets led to a destruction of red cells and thus to anemia. They went so far as to postulate that it was the fatty acids which broke down the red cells, basing this theory partly on the marked hemolytic action of oleic acid in vitro. That the erythrocytes were not destroyed in the circulating blood was proved by the absence of hemoglobinuria. Most likely the destruction must take place in the liver and spleen; that is. in those centers where normal blood destruction occurs. To prove this they looked for and found deposits of hemosiderin in the liver and spleen. Further, to establish this hypothesis they tried to show that there was evidence of excessive blood destruction. This link in the chain of evidence was furnished by Glanzman,[1] who published results showing excessive excretion of urobilinogen in the stools of children suffering from alimentary anemia.

Glanzman's results, however, comprise but a few cases, and the method used by him is open to question. He apparently determines only the urobilinogen and not the urobilin. This would necessarily lead to great error since the one substance may be transformed into the other in the intestinal canal. Moreover, many of his results seem to be based on the examination of a single day's feces. The excretion of urobilin and urobilinogen is so irregular that very great differences are found in the amounts excreted on consecutive days. To get an adequate idea of the total excretion one must therefore make determinations over a number of days; as many, even, as six or seven.

Although not at all convincing, Glanzman's results are interesting and prompted us to investigate the urobilin and urobilinogen excretion in similar cases.

The method used by us [2] for urobilin determination was that of Wilbur and Addis.[3] This method is admittedly a rough one, and will certainly fail to show very small changes in the amount of urobilin

1. Glanzman: Jahrb. f. Kinderh. **84**:95, 1916.

2. A Smith & Haensch spectroscope, with adjustable slit, was used. Illumination was obtained by enclosing a Mazda electric bulb in a box completely closed, except for a small opening for insertion of the spectroscope.

3. Denzer, B. S., and Merritt, K. K.: The Urobilin Content of the Stools of Normal Infants, Am. J. Dis. Child. **27**:297 (April) 1924.

present in the stools. (By urobilin is meant the sum total of urobilin and urobilinogen found in the stools.) For larger variations it has proved itself a good method. Since many factors, such as the destruction of urobilin in the intestine, or its reabsorption from the intestine, combine to make the total urobilin excretion only roughly proportional to the amount of blood destruction, only a very pronounced increase in the urobilin found in the stool may be accepted as proof of a hemolytic process.

As no figures were available for urobilin excretion of normal children over 1 year of age, preliminary examinations of normal children were made. The results are shown in Table 1. The variations are wide, which was to be expected when obtained by the method of Wilbur and Addis. However, only the upper limit of normal is of importance in the consideration of the urobilin of the stools as an indicator of the degree

TABLE 1.—*Excretion of Urobilin in the Stools of Normal Children*

Case	Period of Observation, Days	Age	Average Total Urobilin Values
1	6	18 months	287
2	6	2 years 2 months	500
3	5	3 years	147
4	6	3 years 6 months	283
5	7	3 years 6 months	428
6	3	5 years	733
7	4	6 years	750
8	6	6 years	798
9	6	6 years	1,000
10	6	7 years	1,167
11	6	8 years	870
12	6	10 years	1,180
13	7	11 years	1,345
14	6	11 years	775

of blood destruction. It may be said, then, that under 6 years of age the normal urobilin does not exceed 800 dilution units, and between 6 and 11 years it does not exceed 1,400 units.

We have examined, in all, twenty-one children suffering from various forms of anemia and from diseases of the hepatosplenic system. Table 2 shows the various illnesses and the laboratory findings. It will be seen that only one case showed a really definite increase in the urobilin excretion. This patient was suffering from typical congenital hemolytic jaundice. The urobilin excretion was more than five times the normal amount and following splenectomy it dropped promptly to almost within normal limits. There were three cases that showed a slightly excessive excretion (the last three in Table 2). The urobilin values in these cases were considerably less than double the normal amount. Two were obscure conditions, affecting liver and spleen, and the third was Gaucher's disease. So far as we know, excessive blood destruction has not been found previously in Gaucher's disease, and a greater number of cases would have to be studied to determine its

TABLE 2.—*Excretion of Urobilin in Alimentary Anemia and Other Pathologic Conditions*

Name	Sex*	Age	Period of Observation, Days	Urobilin Values	Hemoglobin, per Cent.	Diagnosis	Remarks
Alimentary Anemia							
L. B.	♀	18 mo.	5	165	30	Anemia, rickets, nasopharyngitis	Diet: milk and cereal. Repeated upper respiratory infection probably also an etiologic factor
R. R.	♂	15 mo.	12	391	40	Nasopharyngitis, rickets	Slow improvement under iron therapy
E. O.	♂	2¾ yr.	6	184	24	Anemia	Diet: milk and orange juice. Refused all solid food. Premature baby. Predisposition (prematurity) and food only etiologic factors. Marked improvement with iron; hemoglobin to 70 per cent. Systolic cardiac murmur disappeared
G. K.	♀	9 mo.	4	86	14	Anemia	Diet: milk, water and sugar until few weeks previously; cereal and little vegetable added. Full term. Pertussis at four months. Blood transfusion and iron given. In two weeks hemoglobin 40 per cent.
Congenital Hemolytic Jaundice							
E. S.	♀	6 yr.	7	4,862	45	Congenital hemolytic jaundice	Spleen removed. Normal urobilin about 1,400 or less
Postoperative			6	911			
Miscellaneous Conditions							
J. B.	♂	4 yr.	6	247	59	Rheumatic carditis	Normal urobilin. Progressive anemia. Hemoglobin fell to 48 per cent.
M. S.	♀	8 yr.	7	767	68	Malignant endocarditis	Normal urobilin. Progressive anemia. Hemoglobin fell to 47 per cent.
M. D.	♂	2¾ yr.	6	575	39	Anemia following pneumonia	Urobilin normal. Estimations made after pneumonia. Progressive anemia during and after pneumonia
G. N.	♀	12 yr.	7	864	39	Endocarditis; etc.	Normal urobilin. Large spleen and liver
R. H.	♀	10 mo.	8	148	60	Tuberculosis	Normal urobilin. Progressive anemia. Hemoglobin fell to 49 per cent.
R. P.	♀	10 yr.	6	1,174	..	Trichinosis	Normal urobilin
M. P.	♀	8 yr.	6	925	..	Trichinosis	Normal urobilin
M. P.	♀	10 yr.	7	584	35	Aplastic anemia(?)	Normal probilin
A. S.	♂	6 yr.	7	682	74	Hemorrhagica purpura	Normal urobilin
F. F.	♀	8 yr.	6	1,070	62	Purpura hemorrhagica	Normal urobilin. No decrease, postoperative splenectomy
Postoperative			9	1,079			
J. R.	♂	6½ yr.	6	927	96	Splenomegalic cirrhosis (?)	Normal urobilin
H. P.	♀	9 yr.	4	425	93	Gaucher's disease (?)	Normal urobilin. Diagnosis not proved; neither splenectomy or puncture done
E. G.	♂	8 yr.	7	870	..	Hepatic lymphangioma (?)	Normal urobilin
Slightly Increased Urobilin Values							
F. K.	♂	2½ yr.	8	816	75	Splenomegalic cirrhosis (?)	Normal urobilin value not above 800
M. R.	♂	9 yr.	6	2,233	72	Splenomegaly (?)	Normal urobilin value not above 1,400. Diagnosis never established. Case not followed
F. R.	♀	3 yr.	6	1,352	66	Gaucher's disease	Normal urobilin value not above 800. Spleen removed; proving diagnosis
Postoperative			7	842	82		

* In this column, ♀ indicates female, ♂ male.

significance. Possibly any extensive enlargement of the spleen might be sufficiently associated with its blood destructive function to account for the slightly higher values found in these three cases.

In the four cases which we have grouped under the heading of alimentary anemia, no increase in urobilin excretion could be found. This may be due, possibly, to the methods employed, since the blood destruction may proceed at a very slow rate producing a smaller amount of urobilin in the stool at any one time than the method is able to show. It would seem, however, that if an excessive blood destruction accompanied the severe types of infantile anemia, a patient such as G. K. should have presented some evidence of increased urobilin in the stool. This infant with a hemoglobin percentage of 14 failed to show even a slight increase in the urobilin excretion. It seems fair to conclude, then, that rapid and excessive blood destruction is not an important factor in the anemias of infancy (the chlorotic and alimentary anemias).

SUMMARY

1. The sum of the urobilin and urobilinogen excretion in the stools of normal children, obtained by the method of Wilbur and Addis, is less than 800 dilution units for children under 6 years of age; and less than 1,400 units for children under 11 years of age.

2. There is no evidence of excessive blood destruction in the anemias of infancy as indicated by the urobilin excretion in the stools, determined by the method of Wilbur and Addis.

THE CALCIUM CONTENT OF BREAST MILK IN RELATION TO RICKETS*

L. R. DeBUYS, B.S., M.D.
AND
L. VON MEYSENBUG, M.D.
NEW ORLEANS

The rôle of the calcium ion in the metabolism of rickets has for a good many years formed the keystone of the arch in the study of this disease. The conception, recently advanced by Howland and his associates, of the existence of two forms of rickets, the low calcium and the low phosphorus types, is based chiefly on the chemical study of the blood.

Experimentally, the feeding of low phosphorus diets to animals leads to the production of true rickets, whereas low calcium diets lead not to true rickets, but to osteoporosis. It is a fact that in all forms of rickets the body as a whole shows a marked lowering of its calcium content.

Recently, one of us [1] has shown that in the breast milk on which babies develop rickets there was no reduction in the inorganic phosphate constituents, and it seemed worth while to study also the calcium content. To this end mother's milk was obtained from those attending the newly born service of Touro Infirmary, simultaneous observations being made on the infants and in a few instances the clinical examinations were checked by roentgenograms of the wrists. Where, however, the roentgen ray showed no evidence of rickets, while the clinical findings indicated its presence, we have given preference to the clinical evidence, for we agree with Hess [2] that the roentgen ray frequently lags behind the clinical examination in furnishing evidence of the earliest beginnings of rickets.

It must be stated that all the infants in this study were receiving, in addition to their regular nursings, a daily ration of cod liver oil emulsion (one coffeespoonful three times a day). It might be said, therefore, that those infants who developed rickets, in spite of cod liver oil administration, did so on a very gross deficiency of the essential element in the breast milk, if such a deficiency exists at all.

---

* Received for publication, Feb. 27, 1924.

* From service of the newly born, Touro Infirmary, and the School of Medicine of Tulane University of Louisiana.

1. Von Meysenbug, L.: The Inorganic Phosphate Content of Breast Milk of Mothers with Normal and with Rachitic Infants, Am. J. Dis. Child. **24**:200 (Sept.) 1922.

2. Hess, A. F.: Newer Aspects of the Rickets Problem, J. A. M. A. **78**:1177 (April 22) 1922.

METHOD

The milk was secured as uniformly as possible from all mothers in the following way: the infant was allowed to nurse one breast for ten minutes, at the end of which time approximately ½ ounce (15 c.c.) of the strippings was expressed manually into a clean, dry container. An equal quantity was obtained of the foremilk from the other breast, the two thoroughly mixed and kept in the refrigerator until analyzed.

The calcium determinations were carried out as follows: 10 c.c. of milk were pipetted into a 20 c.c. volumetric flask containing about 6 c.c. of 20 per cent. trichloracetic acid (calcium free) and heated in a boiling water bath from fifteen to twenty minutes until a brownish color indicated the caramelization of the lactose, when coagulation of the proteins was usually complete. The flask was cooled and made up to volume. Filtration through double acid washed filter paper gave a crystal clear, slightly yellowish filtrate. Five cubic centimeters of

TABLE 1.—*Normal Babies*

Date	Patient	Age	Ca, Mg. per 100 C.c. Milk	Date	Patient	Age	Ca, Mg. per 100 C.c. Milk
12/ 9/22	M. G.	14 days	32.0	1/30/23	G. R.	1 mo.	35.6
12/30/22	J. S.	4 mos.	31.3	2/ 1/23	A. M.	8 wks.	37.4
12/30/22	C. A.	14 mos.	28.7	2/ 1/23	H. A.	2 mos.	35.4
1/ 2/23	E. P.	5 mos.	30.4	2/15/23	E. M.	2 mos.	39.5
1/ 4/23	D. McD.	4 wks.	32.0	3/ 6/23	C. M.	7 mos.	24.3
1/ 9/23	C. D.	5 wks.	31.0	4/ 5/23	E. S.	4½ mos.	31.9
1/ 9/23	L. W.	6 wks.	33.9	4/19/23	B. G.	5 mos.	34.0
1/16/23	J. V.	8 mos.	32.9	6/21/23	B. D.	2 mos.	40.0
1/20/23	H. T.	5 wks.	32.9	6/28/23	M. H.	2 mos.	31.9
1/27/23	V. H.	8 wks.	30.2				
Average							32.6

filtrate were pipetted into a 15 c.c. graduated centrifuge tube containing 2 c.c. of saturated ammonium oxalate solution and one drop of methyl red. The tube was rotated so as to mix the fluids, and enough of 20 per cent. sodium acetate was added (usually 3 c.c. sufficing) to give a p_H of 5.0 as compared with the color charts of Clark.[3] This p_H is, according to Clark, the optimum for the precipitation of calcium.[4]

The tube was stoppered, set aside over night and then centrifuged at high speed for ten minutes. Supernatant fluid was siphoned off and the precipitate washed with 2 per cent. of ammonia water. The washing and centrifuging were repeated three times. Solution of the precipitate was effected with 2 c.c. approximately double normal sulphuric acid, the tube heated in boiling water and the calcium oxalate titrated against hundredth normal potassium permanganate solution,

3. Clark, Wm.: The Determination of Hydrogen Ions, Baltimore, Williams & Wilkins, 1920.

4. Clark, G. W.: The Micro Determination of Calcium in Whole Blood, Plasma, and Serum by Direct Precipitation, J. Biol. Chem. **49**:487 (Dec.) 1921.

correction being made for the blank. Analysis of known calcium solutions showed this method to be accurate within ± 5 per cent. The results of the milk analysis are set forth in the tables.

Table 1 shows the average of nineteen "normal" milks to be 32.6 mg. per hundred cubic centimeters with extremes of from 23.7 to 40.0 mg.

TABLE 2.—*Rachitic Babies*

Date	Patient	Age	Rickets Clinically	Rickets by Roentgen Ray	Ca, Mg. per 100 C.c. Milk
1/ 9/23	A. P.	5 mos.	++	....	24.1
1/ 9/23	I. S.	5 mos.	+±	....	27.0
1/12/23	W. McC.	9 mos.	++	....	29.4
1/12/23	H. H.	8 mos.	+±	....	22.2
1/12/23	A. J.	4 mos.	+++	....	19.3
1/12/23	R. C.	14 mos.	+	....	20.1
1/16/23	A. L.	3 mos.	+	....	22.4
1/16/23	A. B.	4 mos.	±	....	26.2
1/16/23	P. T.	2 mos.	+	....	22.4
1/20/23	R. J.	11 mos.	+±	....	28.5
1/20/23	L. J.	5 mos.	+	....	31.5
1/20/23	E. R.	5 wks.	±	....	29.4
1/23/23	J. B.	11 mos.	+	....	23.9
1/25/23	A. A.	4 mos.	±	....	33.9
1/25/23	C. McD.	3½ mos.	+	....	31.0
1/27/23	E. H.	12 mos.	++	....	27.2
1/27/23	E. F.	3 mos.	+	....	29.4
1/30/23	C. M.	4 mos.	±	....	30.3
2/ 1/23	U. G.	2 mos.	+	....	30.6
2/ 3/23	E. J.	4 mos.	±	....	23.8
2/ 3/23	W. B.	8 mos.	+	0	39.6
2/ 3/23	A. H.	3 mos.	±	healing	32.7
2/ 6/23	D. T.	9 mos.	±	±	19.2
2/ 8/23	V. L.	6 mos.	++	+	31.4
2/ 8/23	P. V.	4 mos.	±	0	34.4
2/10/23	D. F.	7 mos.	+	±	20.9
2/10/23	B. C.	7 mos.	+	0	26.9
2/10/23	J. A.	2 mos.	±	0	22.1
2/15/23	E. J.	5 mos.	+±	....	29.1
2/15/23	U. J.	3 mos.	++	0	32.1
2/15/23	M. M.	7 mos.	+	+	26.5
2/17/23	D. S.	3 mos.	+	+	31.7
2/20/23	T. L.	2 mos.	+±	0	33.9
2/20/23	S. E.	8 mos.	+	0	21.0
2/22/23	D. J.	7 mos.	++	....	23.2
2/22/23	A. H.	3 mos.	+	0	26.5
2/22/23	P. B.	2 mos.	++	0	23.0
2/24/23	V. B.	7 mos.	+	0	26.5
2/24/23	K. M.	3 mos.	±	....	35.5
2/27/23	S. S.	6 mos.	±	0	36.3
3/ 1/23	W. S.	5 mos.	+	+	27.6
3/ 1/23	W. B.	4 mos.	++	+	18.4
3/ 3/23	D. L.	7 mos.	+	....	19.9
3/ 8/23	E. R.	10 mos.	+	+	27.3
3/ 8/23	H. T.	3 mos.	+	+	27.8
3/10/23	P. T.	5 mos.	++	±	30.2
3/29/23	R. E.	3 mos.	+	0	33.1
5/ 3/23	H. R.	5 mos.	+	....	24.2
5/17/23	G. M.	2 mos.	++	....	31.6
5/17/23	E. S.	5½ mos.	+	....	30.0
6/21/23	V. C.	3½ mos.	±	....	28.0
Average					27.5

The average of the "rachitic" milks, as collected in Table 2, is 27.5 mg. with extremes of from 18.4 to 39.6 mg. With a view to correlating the severity of the rickets with the milk calcium we have calculated the averages as follows: When the clinical evidences of rickets is ± (based chiefly on the degree of the beading) the average is 29.3 mg. where rickets is + it is 26.8 mg.; for + ± and + +, 26.8 mg. The only + + + case had 19.3 mg.

TABLE 3.—*Averages for Different Periods*

Period	Number of Analyses	Ca, Mg. per 100 C.c.
1 – 3 months	30	31.1
4 – 7 months	28	28.0
8 months – 1 year	12	26.2

TABLE 4.—*Calcium Content of Mature Breast Milk*

Author	Ages	Ca, Mg. per 100 C.c.
Schloss	2 – 6 mos.	29.7
Pelka	.....	33.5
Holt, et al.	1 –10 mos.	33.3
Abderhalden	2 – 3 mos.	34.6
Blanberg	.....	27.9
Denis *	.....	29.5
Von Meysenbug	1 –12 mos.	32.6

* Unpublished work.

TABLE 5.—*Averages for Different Periods* *

	Number of Analyses	Ca, Mg. per 100 C.c.
Colostrum (1-12 days)	5	31.6
Transition (12-30 days)	6	29.0
Early mature (1-4 months)	9	34.5
Middle mature (4-9 months)	8	32.5
Late milk (10-20 months)	10	27.7

* Computed from Table of Holt et al.[5]

TABLE 6.—*Average of Milks of White and Colored Mothers*

White				Colored			
32.0	30.6	35.6		30.4	32.8	23.8	23.0
31.3	39.6	36.3		30.9	28.5	32.7	18.4
23.8	34.4	27.6		24.1	31.5	19.1	19.9
33.2	26.9	27.3		27.0	29.4	31.4	33.1
30.0	22.1	30.2		33.9	23.9	20.9	24.3
32.9	26.5	32.0		22.2	33.9	29.1	27.8
30.3	33.9	30.0		19.6	31.0	39.5	34.0
37.4	26.5	40.0		20.1	27.2	32.1	24.2
35.4	26.6	28.0		22.4	29.4	31.7	31.6
				26.4	30.2	21.0	31.9
Average.....		31.1 mg.		22.4	35.6	23.2	
				Average.....			27.3 mg.

In Table 3 we have grouped the milks according to the ages of the infants (stage of lactation). This table includes all the milks, "normal" as well as "rachitic."

Table 4 comprises breast milk calcium as found by different investigators, taken from Holt.[5]

For comparison with our results of analyses at progressing stages of lactation we have inserted Table 5 taken from Holt.

In Table 6 we have grouped all the milks of white and colored mothers separately and the average of the two show 31.1 mg. for milk of the white mothers and 27.3 mg. for the milks of the colored mothers.

COMMENT

It will be seen from the Tables that milks from some of our severest cases of rickets showed calcium content well within the range for the "normal" milks, two being higher than the normal average. On the other hand, nowhere do we find in the controls the low extremes that we find in the rachitic group. Whether or not some of our rachitic cases showing high milk calciums belonged in the low phosphorus group could only have been determined by calcium and phosphorus determinations of the infants' blood.

We do not feel that the routine administration of cod liver oil to all the infants in this study has vitiated our results, for the infants developed rickets in spite of such administration, and obviously giving cod liver oil to the infant could in no way affect the calcium content of the mothers' milk.

As we have secured milks from only nineteen control cases, and as we have fifty-one test milks, it was thought that comparison of the two groups might not be fair. We, therefore, averaged the first nineteen milks of the rachitic group and found it to be 26.7 mg. calcium per hundred cubic centimeters, an average even lower than that of the entire series of fifty-one cases.

As colored babies are so prone to develop rickets we thought that there might be some reduction of the milk calcium in colored mothers. In a recent study of Burhaus and Smith[6] this was shown to be the case, the average for the milks of the white mothers being 30.79 mg.; for the milks of the colored mothers 25.41 mg. per hundred cubic centimeters. Our averages are 31.1 mg. for the white race, 27.3 for the colored race.

---

5. Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10**: 229 (Oct.) 1915.

6. Burhaus, C. W., and Smith, D. N.: The Inorganic Constituents of Human Milk with Particular Reference to Racial Variations, Am. J. Dis. Child. **26**:303 (Oct.) 1923.

SUMMARY

In a study of the calcium content of breast milk we have found the average of "normal" milks to be 32.6 mg. per hundred cubic centimeters, with extremes of from 23.7 to 40.0 mg.

The "rachitic" milks averaged 27.5 mg. with extremes from 18.4 to 39.6 mg.

Grouping the milks according to the age of the infant we found the calcium content diminishes as lactation progresses.

The calcium content of milk from the white race as compared with that of the colored shows a reduction in the latter race.

SUBACUTE INTUSSUSCEPTION *

VICTORIA C. A. BERGSTROM, M.D.

NEW YORK

The term subacute, in relation to intussusception, commonly describes a type of case in which symptoms have existed for at least a week, yet does not present the striking symptomatology manifested by the typical acute cases. Certain of these subacute cases offer difficult problems in diagnosis. As detailed descriptions of such cases in infants and young children are but rarely presented, the report of the four following cases seems of sufficient interest to merit publication.

REPORT OF CASES

CASE 1.—*History.*—H. G., a girl, the second of two children, was breast fed exclusively for one month, and then because of failing lactation, five supplementary feedings of whole milk and barley-water mixtures were given in addition to three nursings. At 4 months of age the infant was brought to the outpatient department of the Babies' Hospital because of vomiting and diarrhea. The symptoms yielded promptly to dietary changes and the child gained normally in weight. At 6 months of age the weight was recorded as 14 pounds (6,350 gm.).

Present Illness.—On July 17, 1922, when 6 months of age, the infant was brought to the outpatient department by the mother, who stated that eight days previously the child had vomited and had passed four stools of bright red blood mixed with mucus, associated with severe colicky pains. The family physician in attendance at this time treated her with "powders." The bowels became constipated and enemas resulted in "black stools."

On the day of admission to the hospital the colicky pains were still present, but the patient did not look acutely ill nor was she dehydrated. The mother stated that constipation was present and that food was refused. A small greenish fecal stool of normal consistency was passed at the time of examination. This gave a positive guaiacum test for blood. Under ether anesthesia a sausage-shaped mass was readily felt in the right lower quadrant of the abdomen. The white blood cells numbered 23,000; the polymorphonuclears were 69 per cent.

Operation was immediately performed by Dr. Richard Bolling. Under ether anesthesia a right rectus incision was made, and an intussusception 12 inches (30 cm.) long was found. This began at the ileocecal valve and involved the appendix. There was some inflammation present but no necrosis was seen, and the intussusception was easily reduced. Two ecchymotic spots were seen in the mesentery. The ileum was sewed to the cecum for a distance of about 2 inches (5 cm.) with the idea of preventing recurrence. The incision was then closed and the patient made an uneventful recovery.

The infant has been seen repeatedly since the operation and appears to be normal in every respect.

CASE 2.—A. L., a boy, aged 6 months, was admitted to the Babies' Hospital, March 7, 1922.

---

* Received for publication, Feb. 11, 1924.

* Report of Four Cases from The Babies' Hospital Dispensary.

Previous History.—He was the youngest of four children, of healthy parents, born at term, with birth weight recorded as 9 pounds (4,082 gm.). He was nursed up to the onset of the present illness and throve in a normal fashion.

Present Illness.—Sixteen days prior to admission to the hospital the infant became suddenly ill. Bloody stools were noted at the onset, after which their character changed to a mixture of blood, mucus and feces, subsequently containing curds and mucus. Since then there had been six or seven watery stools daily but none contained any blood. The patient had been prostrated from the onset. The attending physician thought his symptoms were due to intestinal intoxication. His condition seemed to improve until five days before entering the hospital, when high fever began, which the physician believed to be due to meningitis. Prostration became more marked. This was associated with dyspnea and persistent vomiting of food and greenish material.

A diagnosis of peritonitis was then made and the child was referred to the Babies' Hospital.

Physical Examination.—On admission to hospital the child was moribund. The features were pinched, the expression was anxious and the true facies abdominalis was seen. The respirations were rapid; the vomiting of bile stained material occurred repeatedly. The temperature was 102.2. The abdomen was tense and much distended. The clinical diagnosis was general peritonitis. The infant died one hour after admission to the hospital.

Necropsy was performed by Dr. Martha Wollstein with the following findings: On opening the abdomen, the presenting loops of intestine were adherent to the abdominal wall and to each other by fibrinous adhesions which were easily broken down. The peritoneal cavity was found to be full of greenish, odorless pus in which there were large flakes of fibrin. There was an ileocecal intussusception present, into which the base of the appendix was disappearing. The outer surface of the tumor, which measured 7 by 4 cm., was red in color, but showed no signs of gangrene and was easily reducible. The colon below the tumor contained yellow, pasty feces and the small intestine above contained very loose fecal matter. The stomach contained bile-stained material; its mucosa and that of the duodenum were normal.

The anatomic diagnosis was ileocecal intussusception—not complete.

The history of sudden onset sixteen days before death with stools containing fresh blood, subsequently becoming fecal, made it appear that the original condition had been intussusception without complete obstruction, in which there had been a spontaneous, incomplete reduction.

Case 3.—E. G., a boy, aged 8 months, the youngest of three children, of healthy parents, was born at term, after a normal birth. He had been nursed every three hours, had gained in weight normally, and had never been ill.

Present Illness.—Eight days before admission to hospital the infant became restless, and subsequently passed four loose stools containing mucus. On that day he slept fairly well but during the night on three occasions vomited small amounts of food. The following morning he refused food, and again was quite restless and vomited a considerable amount of brown-stained material. Later in the morning, a large amount of bright red blood "gushed from the bowels," which was stated to have saturated three diapers and the mattress. No evidence of pain was noted and the child became drowsy. A physician called thought it was a case of "bloody dysentery" and prescribed medication. The following day the patient passed two bloody stools. Another physician was called five days later, but during this time there was a daily stool containing some blood. The day prior to admission to the hospital the patient had a normal stool which did not contain blood.

On the day of admission he had another blood stained stool, and vomiting was observed at four different times. It was also stated that he showed signs of great pain.

Physical Examination.—The infant, when presented for admission, was critically ill, in a comatose state, with ashy countenance, sunken eyes rolling from side to side, and a sunken fontanel admitting two finger tips. The abdomen was soft; the liver and the spleen could not be palpated. Although no definite mass could be palpated nor could any be felt by rectum, the whole picture of the illness and the manner of its development suggested the diagnosis of an invagination of the bowel.

Operation was performed by Dr. Bolling, eight days after the onset of symptoms. A right rectus incision was made and an intussusception was found which was markedly edematous. The head of the column was formed by the lower end of the cecum at a point opposite the ileocecal valve.

Immediately after the operation the child was in such good condition that he tried to sit up. Eighteen hours later he began to vomit and the pulse became small. The following day signs of obstruction became manifest with fecal vomiting. No fecal contents were withdrawn on irrigation of the colon. That evening there was a second operation for obstruction, and an ileus was found, the paralysis apparently being of toxic origin. An ileostomy was performed and a catheter was sewed into the ileum. The child remained in a critical condition for several days, but gradually improved and was discharged as cured. He has been seen at regular intervals since his discharge from the hospital and is doing well.

CASE 4.—F. B., a boy, aged 8 years, walked into the outpatient department of the Babies' Hospital, Dec. 29, 1919, complaining of pain in the left side of the abdomen.

The family and past history were negative.

Present Illness.—For one week previous to admission to hospital he had four watery stools daily. His appetite was good. He had had intermittent pain in the abdomen but it was not severe enough to confine him to bed; in fact, he was running about as usual, bending over from time to time as the pain occurred. He had noticed a lump in the left side of abdomen but did not know how long it had been present. He had no symptoms referable to the urinary tract.

On the day before coming to the hospital he noticed that the stool was orange colored, of jelly-like substance; he had not noticed the presence of blood.

Physical Examination.—The boy was very pale. During the examination he vomited twice, and at intervals had severe colic in the left flank and the left lower quadrant of the abdomen.

There were no positive findings except in the abdomen, which was flat and soft. A firm, elongated, movable, slightly tender mass 3 by 2 inches (7 by 5 cm.) was palpated in the left lower quadrant, which followed the course of the descending colon or sigmoid. No other masses or tenderness were elicited. The liver, spleen and kidneys were not palpable.

The urinalysis was negative.

The white blood cells numbered 12,100, and polymorphonuclears were 69 per cent.

A diagnosis of intussusception was made, and the child was referred to the Presbyterian Hospital for operation as he was above the age limit of admission to the Babies' Hospital.

Operation was performed by Dr. Sidney Burnap eight days after onset. We are indebted to the Presbyterian Hospital for the following report: "Under ether anesthesia, an incision 5 inches (12 cm.) long was made through the right rectus, and a sausage-shaped mass was found in the left lumbar region extending as low as the brim of the pelvis upward toward the splenic flexure into the transverse colon. The omentum was adherent to it, with fresh adhesions, in the region of the splenic flexure. On reduction of the invagination, at the terminal portion corresponding to the part at which the intussusception began, which was situated close to the junction of the transverse colon with

the splenic flexure, the colon was found to be markedly edematous and congested. This condition, however, subsided greatly on the application of hot towels. No necrosis was seen, the ileocecal junction was found to be normal, and the abdomen was closed."

The patient made an uneventful recovery, and is seen at regular intervals. He is in excellent health, although he complains occasionally of a slight vague pain in the abdomen.

COMMENT

The symptoms of acute intussusception in infants need no review. When a healthy nursing infant in the middle third of his first year suddenly develops pain of a paroxysmal character, accompanied by vomiting whenever food is taken, one naturally thinks first of intussusception. If bright red blood is passed by rectum it only remains to palpate the tumor to make certain of the diagnosis. The symptoms of the subacute type resemble the acute in most particulars except that they are more moderate in their manifestations, and for that reason the diagnosis may be unduly delayed. Three of the four cases here presented were treated for dysentery before admission to the hospital, and it is readily understood how such an error might be made unless the physician had the actual condition in mind. Nursing infants who have always been well are not immune to dysentery; and colic, vomiting, bloody stools and collapse may all be present when it occurs. Increase in pain, more frequent recurrence of the attacks of colic with profuse evacuation of blood and mucus following collapse point to invagination. General anesthesia is frequently necessary to secure sufficient muscular relaxation to establish the presence of a tumor. The vomiting in the subacute patients is not continuous, the loud shrieks due to pain are not noted, usually the constitutional disturbance is not severe, and the patient may escape careful abdominal examination until the symptoms of complete obstruction have appeared.

SUMMARY

Four cases of intussusception from eight to sixteen days' duration are presented, three of which were ileocecal and one of colonic invagination. The first three occurred in infants from 6 to 8 months of age, and the fourth in a boy aged 8 years.

The three infants had been nursed from birth, and except for slight digestive disturbances had never been ill. At the onset of the present illness the three infants had bloody stools, varying from a few tablespoonfuls in two cases, to enough to constitute a profuse hemorrhage in the third case. There was vomiting and pain at this time and subsequently the stools became watery. On physical examination, in two of the patients, a tumor was found in the right and left lower quadrant,

respectively, of the abdomen. Operation, performed on two of the patients eight days after onset, resulted favorably. The third case came to necropsy sixteen days after onset.

In the boy aged 8 years, no fresh blood had been noticed at any time in the stools. The colicky pain, vomiting and the tumor pointed to an invagination of the bowel. Operation, performed eight days after the first attack of pain and vomiting, resulted in his complete recovery.

SO-CALLED IDIOPATHIC CARDIAC HYPERTROPHY IN INFANCY*

GEORGE L. CARRINGTON, M.D.
BRYN MAWR, PA.
AND
EDWARD B. KRUMBHAAR, M.D.
PHILADELPHIA

Marked hypertrophy of the heart in infants and young children, without sufficient anatomic changes at autopsy to explain the hypertrophy on the basis of ordinary pathologico-physiologic processes, has been reported in about twenty cases. Below is the report of a case that we wish to add to the series already recorded.

REPORT OF CASE

History.—D. M., a girl, white, aged 10 months, was admitted to Bryn Mawr Hospital, June 14, 1922. The family history was negative. The father and mother, each in the thirties, were physically healthy. Five other children were living and well. There had been no miscarriages. The patient had been breast fed for less than six months; she had always been puny, but never edematous. Nothing was known about infections.

Present Illness.—Until a few days before admission the patient seemed to be in a normal condition. She then became sick and feverish, with a temperature of 102, pulse 140, and respiration 50. On admission, percussion of the whole left chest gave a flat note. There were many râles on the left side posteriorly. The heart sounds were normal. A diagnosis of pneumonia was made. The temperature returned to normal within four days of admission, and the patient seemed fairly well. The percussion note continued permanently flat over the whole left chest. Roentgen-ray examination showed a greatly enlarged heart. The pulse rate dropped with the temperature from 140 to 110, but never fell below this level. Respirations continued from 30 to 50 until the terminal illness.

Physical Examination.—On August, 10, the weight was 15 pounds 10 ounces (7.087 gm.). The measurements were: length, 70 cm.; head, 44 cm.; chest, 44 cm.; abdomen, 42 cm. The anterior fontanel admitted one and one-half fingers. The eyes reacted to light. The glandular system showed no enlargements. The liver and spleen were palpable. The chest was asymmetrical, bulging over the cardiac area. The left hemithorax measured 1 cm. more than the right at the level of the apex beat. The relative cardiac dulness was percussed into the axilla on the left and on the right extended 1.5 cm. from the midsternal line. The heart sounds were well heard and essentially normal. There were no thrills. The second aortic was greater than the second pulmonic. The lungs were practically clear to percussion and auscultation, except that the breath sounds were diminished over the left chest.

The diagnosis was idiopathic cardiac hypertrophy (so-called).

Course in Hospital.—On account of the persistent flatness in the left chest, on July 20 a needle had been inserted in the mid-axillary line without result. It probably entered the compressed lung and the persistent flatness was pre-

* Received for publication, Feb. 12, 1924.

* From the Byrn Mawr Hospital and the Laboratory of Postmortem Pathology of the Philadelphia General Hospital.

sumably due to the greatly enlarged heart. The patient's condition continued good until a few days before death, when she developed signs of bronchopneumonia that terminated fatally, Aug. 31, 1922.

Necropsy.—A fairly well-nourished white female infant was seen, about 1 year of age. On opening the thoracic cavity the heart appeared to occupy the whole left side of the chest. The left lung was compressed and showed a few areas of congestion.

Heart: The pericardial cavity contained a small amount of bloody fluid with some fibrin but no adhesions. The heart itself was quite large and rather rounded. The hypertrophy was more to the left than to the right. The pericardium was smooth and glistening, except for a milk patch 1 cm. in diameter

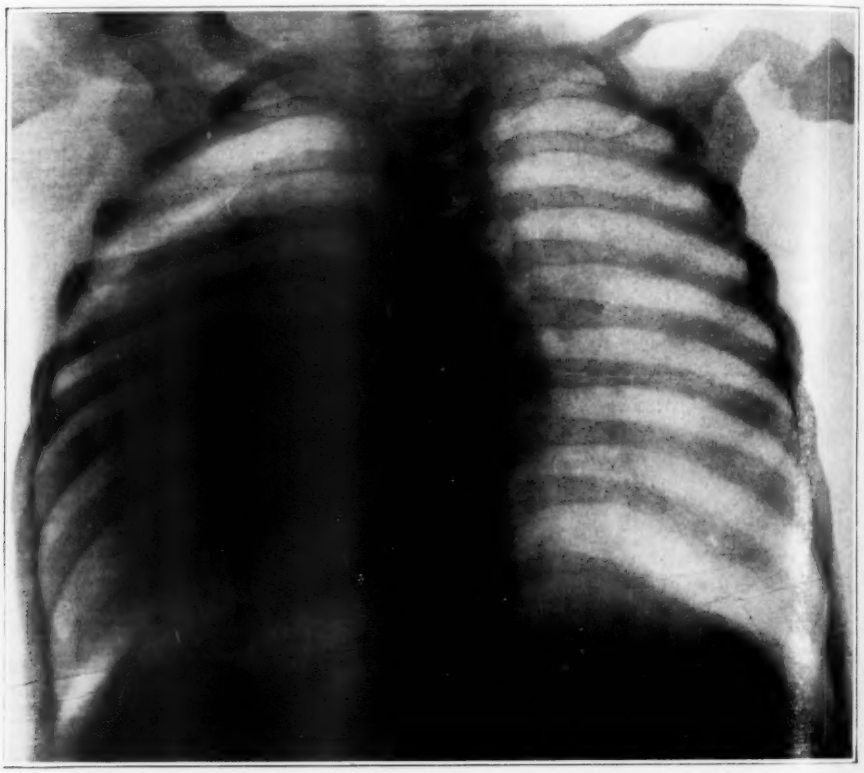

Fig. 1.—Posterior view of thorax of child showing idiopathic cardiac hypertrophy.

near the apex. The subpericardial fat was normal. The diameters were: transverse, 8 cm.; anteroposterior, 5.6 cm.; apex to origin of pulmonic artery, 7.5 cm. Circumference of valves: tricuspid, 6.4 cm.; mitral, 5.8 cm.; aortic, 3.5 cm.; pulmonic, 3.8 cm. Aorta, 3.4 cm. The wall of the left ventricle was from 1 to 1.2 cm., of the right ventricle from 0.4 to 0.6 cm. The weight of the heart was 136 gm.

The right auricle and ventricle were a little hypertrophied but not dilated. The left auricle was both hypertrophied and dilated, and the endocardium uniformly thick and opaque. The chief change was in the left ventricle, which was greatly hypertrophied and dilated and its endocardium was

slightly thickened in the basal portion. A trabeculation was marked and the mural endocardium of the septum was somewhat thickened. A thin abnormal tendon fiber joined the two papillary muscles. Easily detached red and gray thrombi nestled in the trabeculae near the septum. The anterior papillary muscle (normally supplied by the left coronary artery) was streaked with lines, apparently of fibrosis. The valves were all thin and delicate and appeared competent. The ductus arteriosus and foramen ovale were closed. No difference between the parts of the ventricles supplied by the two coronary arteries was observed grossly.

Fig. 2.—Left ventricle (weight of heart, 136 gm.) of 12 months old infant with idiopathic cardiac hypertrophy.

The left coronary artery arose anomalously from the pulmonary artery just above the posterior cusp. It divided after about 2 cm., the horizontal branch being much the smaller and only traceable for another 2 cm. The more important descending branch was lost a few centimeters before the apex was reached. Although the exact area supplied could not be determined in the absence of injections it was clear that the anomalous artery nourished much less than one half of the heart. It was estimated that it supplied the anterior

portion of the septum, a fringe of the anterior right ventricle and about one half of the left ventricle. This probably included all or part of the anterior papillary muscle of the mitral valve.

Lungs: The left lung was somewhat compressed, with some areas of matting and congestion. Weight: left lung, 68 gm.; right lung, 96 gm.

Thymus: No abnormality noted.

The liver weighed 384 gm. Otherwise there was nothing of note. The gall-bladder measured 2½ by 1 inch. The walls were thickened. The stomach and intestines were normal in appearance. The spleen and kidneys showed no gross abnormality.

Fig. 3.—Right ventricle showing rod in anomalous coronary artery arising from pulmonary artery.

Anatomic Diagnosis.—Idiopathic cardiac hypertrophy, anomaly of coronary artery; bronchopneumonia (terminal).

Histology.—The heart: Sections from various parts of the ventricles showed large fibers, with a tendency to large rectangular nuclei. Many, however, were unduly wavy and separated by a slight amount of fleecy fibrous tissue. They had undergone considerable vacuolar degeneration. There was no increase in pigmentation or fragmentation. There was distinct increase of old interstitial

fibrous tissue in sections from the anterior papillary muscle of the mitral valve and from the anterior portion of the septum. This was diffuse, rather than perivascular and nearer the endocardium than the pericardium. The parenchymatous degeneration (loss of striae and vacuolization) was also most marked in the areas supplied by the anomalous artery. There were no abnormalities in the coronary vessel walls. The diagnosis was parenchymatous degeneration of myocardium and slight, localized myocardial fibrosis.

The lungs: Conglomerate areas of bronchopneumonia; alveoli filled with polymorphonuclear cells (many degenerated) also large mononuclear cells and débris; the bronchi were also full of polymorphonuclears. In other areas, heart failure cells and fleecy pink staining material predominated. The diagnosis was bronchopneumonia and edema.

Liver: The strands were more separated than usual and many liver cells had a fleecy, somewhat shredded appearance. The diagnosis was slight passive congestion; cloudy swelling.

In the kidney there were distinct but moderate inflammatory changes in the cortex and medulla. In some areas small round cells replaced the tubules partly or completely, and some of the latter were dilated and contained casts. Numerous vessels were congested. A few glomeruli were shrunken or wholly converted into fibrous tissue, or contained thrombi. The convoluted tubules were much swollen. The diagnosis was chronic mixed nephritis (slight).

COMMENT

It will be noted that there was no urine examination made, and that microscopically the kidneys showed definite pathologic changes. While we do not believe that the renal damage is an important etiologic factor in these cases, we are not prepared to go so far as Howland [1] when he says that nephritis can be dismissed from consideration as a causative factor; especially since in the five cases reported by him there was not one where the study of the kidney was complete and normal. Of the five cases urine examinations were not reported in three cases, one case had albumin, and the fifth had albumin, white and red blood cells. The kidneys in two cases showed gross pathologic changes and in these two no histologic report was included. Yet the cardiac hypertrophy in all of these has been so tremendous, and the pathologic findings elsewhere so meager, that we can hardly conceive of an explanation on the basis of the ordinary pathologico-physiologic processes of nephritis.

More important in the present case is the anomalous origin of the left coronary artery from the pulmonary artery. The nourishment of a considerable part of the cardiac musculature with venous blood cannot be without significance, and yet here the hypertrophy of the myocardium apparently occurs regardless of its source of nourishment, and the degenerative changes of the anomalously supplied muscle seem to be insufficient causes for the tremendous hypertrophy.

---

1. Howland, J.: Idiopathic Hypertrophy of the Heart in Young Children, in Contributions to Medical and Biological Research, Dedicated to Sir William Osler, in Honor of His Seventieth Birthday, July 12, 1919, by his pupils and co-workers, Johns Hopkins Press, 1919.

The explanations offered for this condition by various writers at different times have been: (1) Enlarged thymus; (2) prolonged pertussis or pulmonary disease such as atelectasis or pneumonia; (3) congenital malformation of heart or great vessels; (4) marked rickets of the thorax; (5) diffuse rhabdomyoma of heart (Virchow [2]); (6) a chemical stimulus in the blood; (7) excessive stimulation from the chromaffine system (Hedinger [3]); (8) dilation and hypertrophy following lack of sufficient secretion of the chromaffine system (Michaud [4]); (9) some disturbance of the intra-uterine circulation.

Any comment on these suggested causes in this case would be purely speculative in the present state of our knowledge, and would add nothing of value. There are a few facts, however, that are worth noting about the condition: (1) it is at least sometimes congenital, as two cases have been reported in stillborn infants; (2) some patients have not shown symptoms until they were from 2½ to 4½ years of age, which would make a late hypertrophy seem possible; (3) the break in compensation is surprisingly disastrous, considering the fact that there is hypertrophy without marked or extensive degeneration of the heart muscle fibers; (4) it is not established whether the increase in the size of the heart is due to hypertrophy of the existing fibers, hyperplasia, or both; (5) such factors as slight nephritis and anomalous origin of a coronary artery, as in the present case, are not considered adequate causative factors; (6) the condition would appear to be not especially rare, as evidenced by Oberndorfer's [5] having seen five cases in one year. Congenital rhabdomyoma of the heart is such a different affair that it need not be considered further here.[6]

It is interesting to note that in the case we report there were evidences both of a moderate nephritis and of pulmonary disease. The renal changes though of unknown origin, were thought to be of relatively short duration and not to have played an important part in the cardiac hypertrophy. The rôle of the anomalous coronary and the slight myocardial fibrosis, though unimportant, must still be considered. The pneumonic signs that were present on admission were probably due to a mild infection occurring in an area of the lung that had been compressed by the enlarged heart, rather than the pulmonary infection being an important factor in the cardiac hypertrophy. The signs of a terminal bronchopneumonia were found at necropsy. Certainly none of these factors would ordinarily account for the hypertrophy of the heart from a normal size of from 35 to 40 gm. (Vierordt [7]) at the age of 12 months to the weight of 136 gm. found in this patient.

---

2. Virchow: Berl. klin. Wchnschr. **33**:679, 1896.
3. Hedinger: Cor. Bl. f. schweiz. Aerzte **35**:260, 1905.
4. Michaud: Cor. Bl. f. schweiz. Aerzte **36**:779, 1906.
5. Oberndorfer: Verhandl. d. Gesellsch. f. Kinder. 1906, p. 181.
6. Schmincke: Beitr. z. path. Anat. u. z. allg. Path. **70**:513, 1922.
7. Vierordt: Daten und Tabellen für Mediziner, 1906, p. 36, 37.

Howland's article brought the subject up to date in 1919, but is rather difficult of access. Since that time we have been unable to find any new contribution to the subject.

SUMMARY

1. A case of so-called idiopathic cardiac hypertrophy is reported in an infant aged 12 months.

2. A mild nephritis, myocardial fibrosis and anomalous coronary artery (arising from the pulmonary) are discussed as possible causes.

3. It is probable that this condition includes hypertrophies due to various antenatal and postnatal factors, some of which are still unrecognized, and is seldom, if ever, truly idiopathic.

TUBERCULOUS PYOPNEUMOTHORAX IN AN INFANT AGED FIVE MONTHS *

S. G. ROSS, M.D., AND C. T. CROWDY, M.D.

MONTREAL

Pneumothorax as a complication of tuberculosis in infancy is apparently an uncommon condition. This is the opinion of all writers on the subject. Bourne [1] has recently reported a case in which the condition developed in an infant, aged 18 months. To our knowledge this is the youngest patient in whom this complication has been reported. For other reasons, subsequently presented, the case is also noteworthy.

REPORT OF CASE

R. M., a boy, aged 3 months, was admitted to the Pediatric Department of the Royal Victoria Hospital, Jan. 22, 1923, suffering from cough and loss of weight.

Family History.—The patient's father was suffering from advanced pulmonary tuberculosis and living at home with his family. The mother was in poor health but showed no evidence of active tuberculosis. There had been six pregnancies. The first four children died respectively of diarrhea, meningitis, diphtheria and influenza between the ages of 5 months and 3½ years. The family lived in very poor and cramped quarters.

History.—The patient at birth weighed 5½ pounds (2,495 gm.), and appeared healthy. He was breast fed for one month. After that he was fed on proprietary foods and cow's milk dilutions. There were no digestive disturbances.

Present Illness.—The infant "caught cold" two weeks before admission. Since then he had a cough of moderate severity, and had lost weight and vomited occasionally.

Examination.—A well developed and fairly well nourished infant was seen, weighing 8 pounds, 7 ounces (3.9 kg.). He was slightly pale. There was no superficial glandular enlargement. The temperature was 98, pulse 110, respirations 36; the length of the patient was 52 cm.; circumference of the head 35 cm.; of the abdomen, 33 cm.; of the chest, 33 cm. The ear drums were normal. The chest was symmetrical, and the lungs resonant throughout. On auscultation, breath sounds of the normal puerile character were heard. A few large moist râles were heard, which cleared up on coughing. The heart and abdomen were normal. The urine was also negative. Hemoglobin, 70 per cent. White blood count, 16,000; red blood count, 3,600,000.

Course of Disease.—January 25, an intradermal tuberculin test, 1/10 mg., showed a doubtful positive reaction.

January 30, the child did fairly well since admission, and took his feedings well. He had a slight cough.

January 31, the temperature rose to 100 the previous day. Examination of ears showed left otitis media.

---

* Received for publication, Feb. 27, 1924.

* From the Department of Pediatrics, Royal Victoria Hospital, and the Pathological Institute of McGill University.

1. Bourne, G.: Brit. M. J. **1**:526 (April 9) 1921.

February 1, the temperature was 101.3. Double otitis media had developed. Paracentesis of both ear drums was done. The patient also had moderate diarrhea.

February 3, the temperature fell to normal. Both ears were discharging freely, and the patient was losing weight.

February 6, a few medium moist râles were heard in the right axilla. There was profuse aural discharge.

February 7, an injection of intradermal tuberculin, 1/10 mg., showed a definitely positive reaction. The spleen was palpable. Roentgen ray of the chest (Fig. 1) showed a slightly increased density at the root of the right

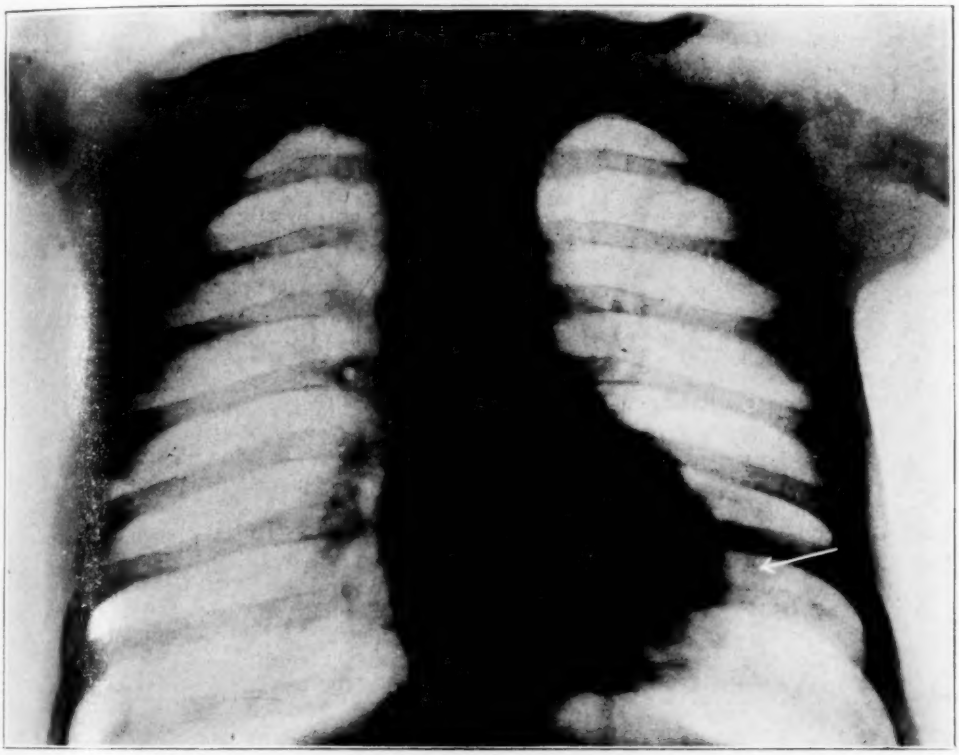

Fig. 1.—Increased density at the root of the right lung, and increased density also in the lower part of the left lung (see arrow).

lung and a patch of increased density in the lower part of the left lung. This patch was probably due to a tubercular focus.

On account of an outbreak of chickenpox in the ward, the patient was discharged. The diagnosis at that time was: (1) Tuberculosis of tracheobronchial lymph nodes; and (2) bilateral suppurative otitis media. It was suspected that there was probably also a primary focus of tuberculosis in the left lung as demonstrated by the roentgen ray. The patient developed varicella ten days after discharge, from which he made a good recovery.

Second Admission.—The patient was admitted to hospital again on April 10, aged 5 months. The cough had persisted during his stay at home and during the week previous to admission had become worse. His weight had remained stationary.

Examination.—The length was now 54 cm; circumference of the head, 37 cm.; of the chest, 34 cm.; of the abdomen, 34 cm. and his weight 8 pounds (3.6 kg.). The temperature was 97, pulse 100 and respirations 30.

The patient was poorly developed and undernourished and appeared ill. His color was pale, with a grayish tinge to the skin. There was slight cyanosis. The skin exhibited scars of recent varicella. There was a definite loss of subcutaneous tissues. No superficial glandular enlargement was noted. The head and eyes were normal. The left ear drum was gray and opaque; it did not bulge, but showed the scar of the old perforation. The right ear drum was gray and opaque, with a small perforation in the posterior half. There was no discharge. The lips were pale and slightly cyanosed. The mouth was normal. The chest was symmetrical. Both sides moved equally on respiration. The percussion note of the lungs was normal throughout. The breath sounds were bronchovesicular in character. In the left upper lobe and high in the left axilla a few fine crepitations were heard. An occasional moist râle was heard in the right lung. The heart was normal. The abdomen rounded, with the liver palpable one finger's breadth below the costal margin. The spleen was palpable. The muscles were weak and of poor tone. The nervous system was normal. The urine was negative. White blood count, 14,000; red blood count, 4,100,000; hemoglobin, 65 per cent. The blood Wassermann was negative.

Course of Disease.—On the evening of admission the patient had a sudden attack of acute dyspnea, with violent coughing lasting several minutes. Examination showed the chest movement was extremely limited in respiration. On percussion the left side of the chest was definitely hyperresonant. The heart dulness was obliterated on the left side and the heart apparently pushed over to the right, the apex beat being felt just to the left of the sternum. Over the left side of the chest the breath sounds were distant and blowing in character. Over the left upper lobe numerous tinkling musical râles were heard. The characteristic coin sound was present. The diagnosis was pneumothorax of the left pleural cavity.

April 10, the general condition was poor, and the respiration was embarrassed. The pulse was 150. The left side of the chest was immobile and showed some bulging with still definite hyperresonance. The breath sounds were distant. The tinkling râles were no longer heard. The coin sound was present, but not so characteristic.

April 12, there was a slight rigidity of the head with a suggestion of Kernig's sign on the left side.

April 13, a discharge from right ear was noted. On auscultation of the chest fine crepitations were heard throughout the right lung.

April 14, the apex of the heart was felt in the midline just below the xiphisternum.

April 15, the patient coughed more. There was dulness on percussion at the left base suggesting fluid.

April 16, the patient appeared weaker. A specimen of sputum obtained from the throat showed the presence of acid-fast bacilli of the morphology of tubercle bacilli. The voice sounds at the lower angle of left scapula were of a distinctly amphoric quality.

April 17, lumbar puncture was attempted, but stopped on account of cyanosis and cessation of respiration.

April 18, an injection of $\frac{1}{10}$ mg. intradermal tuberculin was given, with a decided positive reaction. Dyspnea was more marked; the patient became very weak and died.

Necropsy.—A cisterna puncture was done immediately, and 5 c.c. of turbid fluid was obtained. In the cell count of 1,200, predominantly lymphocytes, no tubercle bacilli were found. The smear showed numerous gram positive lancet shaped diplococci of the morphology of pneumococci (definitely capsulated). The diagnosis was possibly a terminal pneumococcic meningitis. Throughout

the last admission the temperature did not rise above normal. The weight increased from 8 pounds to 8 pounds 6 ounces (from 3.6 to 3.9 kg.)

Roentgen-Ray Reports.—April 11, showed pneumothorax in the left side and a small quantity of fluid in left side of the chest.

April 13 (Fig. 2) showed pneumothorax in the left side, with adhesion of the left lung to the region of the fifth rib at its lateral aspect. The upper part of the pneumothorax extended across to the right lung, reaching about 1 (2.5 cm.) inch beyond the middle line. The trachea and heart were very markedly displaced to the right. Little or no fluid was present. The left pleura showed definite thickening.

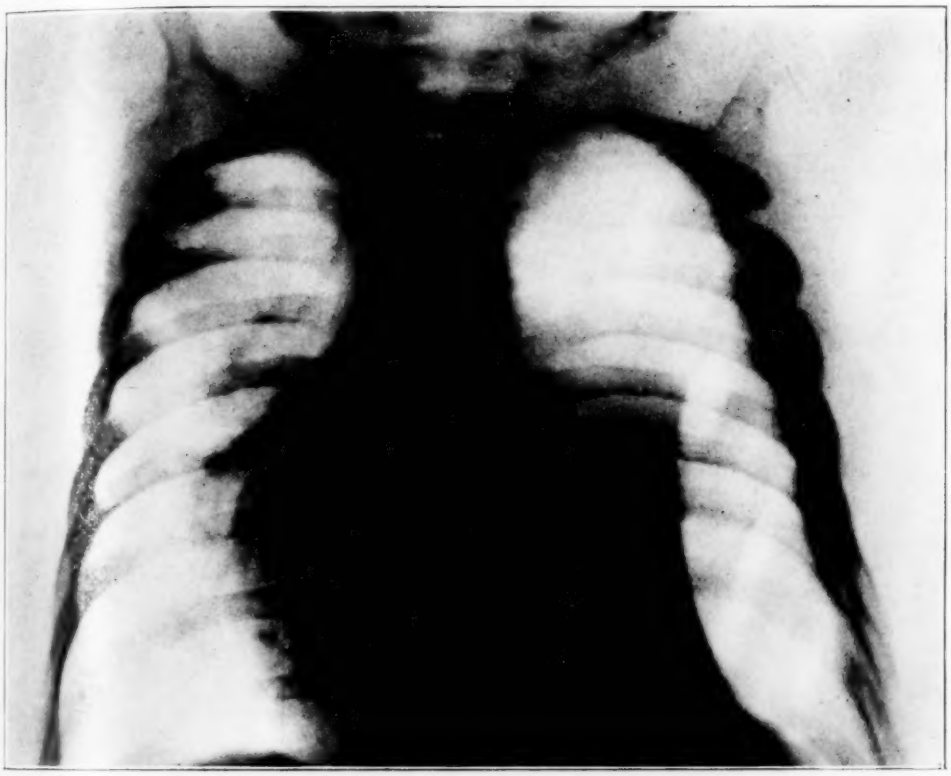

Fig. 2.—Pneumothorax of the left side with lung adhesion. The pneumothorax extends to the right lung.

Clinical Diagnosis.— (1) Pulmonary tuberculosis, (2) tuberculosis of tracheobronchial lymph nodes, (3) tuberculous pneumothorax, and (4) chronic suppurative otitis media.

NECROPSY REPORT OF DR. CROWDY

The chief interest at necropsy centered around the left thorax. Inspection disclosed this side was more prominent than the right. Puncture of the third intercostal space under water demonstrated the presence of air in the left pleural cavity. On opening the thorax, the right lung and heart were displaced to the right, the right lung was compressed and the pleural cavity

Examination.—The length was now 54 cm; circumference of the head, 37 cm.; of the chest, 34 cm.; of the abdomen, 34 cm. and his weight 8 pounds (3.6 kg.). The temperature was 97, pulse 100 and respirations 30.

The patient was poorly developed and undernourished and appeared ill. His color was pale, with a grayish tinge to the skin. There was slight cyanosis. The skin exhibited scars of recent varicella. There was a definite loss of subcutaneous tissues. No superficial glandular enlargement was noted. The head and eyes were normal. The left ear drum was gray and opaque; it did not bulge, but showed the scar of the old perforation. The right ear drum was gray and opaque, with a small perforation in the posterior half. There was no discharge. The lips were pale and slightly cyanosed. The mouth was normal. The chest was symmetrical. Both sides moved equally on respiration. The percussion note of the lungs was normal throughout. The breath sounds were bronchovesicular in character. In the left upper lobe and high in the left axilla a few fine crepitations were heard. An occasional moist râle was heard in the right lung. The heart was normal. The abdomen rounded, with the liver palpable one finger's breadth below the costal margin. The spleen was palpable. The muscles were weak and of poor tone. The nervous system was normal. The urine was negative. White blood count, 14,000; red blood count, 4,100,000; hemoglobin, 65 per cent. The blood Wassermann was negative.

Course of Disease.—On the evening of admission the patient had a sudden attack of acute dyspnea, with violent coughing lasting several minutes. Examination showed the chest movement was extremely limited in respiration. On percussion the left side of the chest was definitely hyperresonant. The heart dulness was obliterated on the left side and the heart apparently pushed over to the right, the apex beat being felt just to the left of the sternum. Over the left side of the chest the breath sounds were distant and blowing in character. Over the left upper lobe numerous tinkling musical râles were heard. The characteristic coin sound was present. The diagnosis was pneumothorax of the left pleural cavity.

April 10, the general condition was poor, and the respiration was embarrassed. The pulse was 150. The left side of the chest was immobile and showed some bulging with still definite hyperresonance. The breath sounds were distant. The tinkling râles were no longer heard. The coin sound was present, but not so characteristic.

April 12, there was a slight rigidity of the head with a suggestion of Kernig's sign on the left side.

April 13, a discharge from right ear was noted. On auscultation of the chest fine crepitations were heard throughout the right lung.

April 14, the apex of the heart was felt in the midline just below the xiphisternum.

April 15, the patient coughed more. There was dulness on percussion at the left base suggesting fluid.

April 16, the patient appeared weaker. A specimen of sputum obtained from the throat showed the presence of acid-fast bacilli of the morphology of tubercle bacilli. The voice sounds at the lower angle of left scapula were of a distinctly amphoric quality.

April 17, lumbar puncture was attempted, but stopped on account of cyanosis and cessation of respiration.

April 18, an injection of $\frac{1}{10}$ mg. intradermal tuberculin was given, with a decided positive reaction. Dyspnea was more marked; the patient became very weak and died.

Necropsy.—A cisterna puncture was done immediately, and 5 c.c. of turbid fluid was obtained. In the cell count of 1,200, predominantly lymphocytes, no tubercle bacilli were found. The smear showed numerous gram positive lancet shaped diplococci of the morphology of pneumococci (definitely capsulated). The diagnosis was possibly a terminal pneumococcic meningitis. Throughout

the last admission the temperature did not rise above normal. The weight increased from 8 pounds to 8 pounds 6 ounces (from 3.6 to 3.9 kg.)

Roentgen-Ray Reports.—April 11, showed pneumothorax in the left side and a small quantity of fluid in left side of the chest.

April 13 (Fig. 2) showed pneumothorax in the left side, with adhesion of the left lung to the region of the fifth rib at its lateral aspect. The upper part of the pneumothorax extended across to the right lung, reaching about 1 (2.5 cm.) inch beyond the middle line. The trachea and heart were very markedly displaced to the right. Little or no fluid was present. The left pleura showed definite thickening.

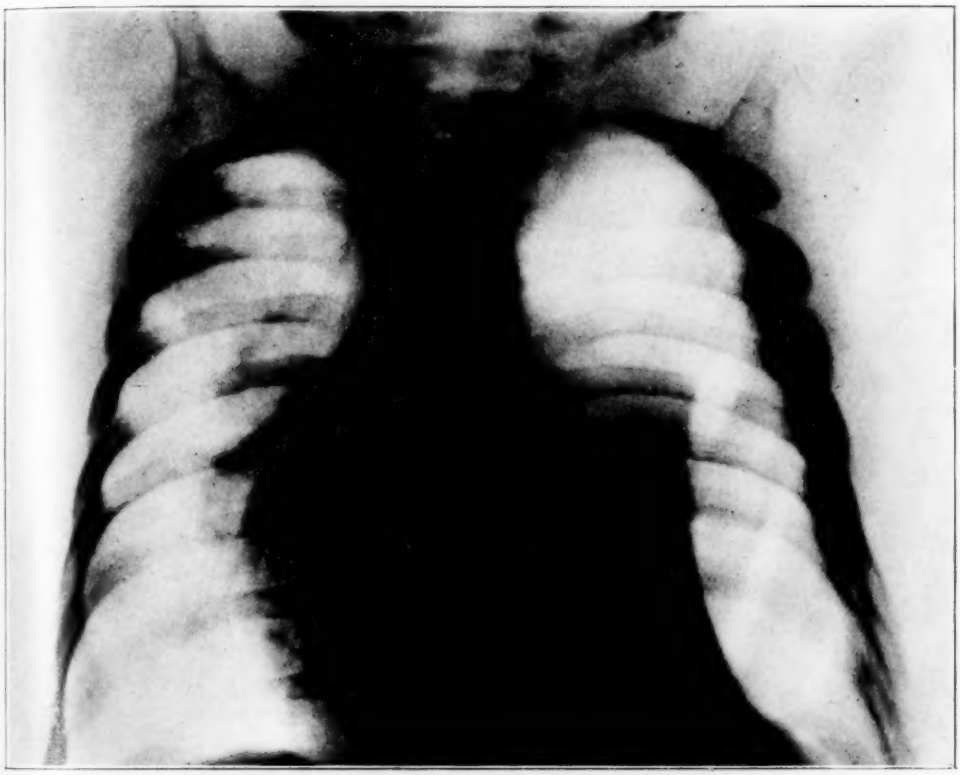

Fig. 2.—Pneumothorax of the left side with lung adhesion. The pneumothorax extends to the right lung.

Clinical Diagnosis.— (1) Pulmonary tuberculosis, (2) tuberculosis of tracheobronchial lymph nodes, (3) tuberculous pneumothorax, and (4) chronic suppurative otitis media.

NECROPSY REPORT OF DR. CROWDY

The chief interest at necropsy centered around the left thorax. Inspection disclosed this side was more prominent than the right. Puncture of the third intercostal space under water demonstrated the presence of air in the left pleural cavity. On opening the thorax, the right lung and heart were displaced to the right, the right lung was compressed and the pleural cavity

contained 2 c.c. of serous fluid. The left lung was collapsed and compressed against the heart and spine, with complete obliteration of the mediastinal part of the pleural cavity and filled approximately only two-fifths of the left thorax. The remainder was represented by a cavity lined by a pyogenic membrane and filled posteriorly with thick, purulent fluid. The anterior part of the cavity was empty and contained air which escaped on puncture. The anterior border of the lung was adherent to the fifth, sixth and seventh ribs just external to the junctions of the corresponding cartilages. This drew the lung out at this point into a fold, and apparently divided the cavity into two parts (Fig. 2), but really only slightly constricting it at this point. The left lung was then removed with the mediastinal tissues, by dissection between the parietal pleura and the ribs. In this way the left thorax was kept intact. On removal, two

Fig. 3.—Perforations in the visceral pleura.

perforations (Fig. 3) in the visceral pleura near the midlateral aspect were visible and these communicated with a pulmonary cavity.

The specimen was preserved in Kaiserling's solution (No. 1) for several months, and in this way a perfect preservation of colors and tissues was obtained. Examination with a probe showed that a main branch of the bronchus communicated with the cavity and section was so planned as to open the trachea, left bronchus and the branch which opened into the pulmonary cavity (Fig. 4). The cut surface showed the following additional interesting points: In the first place, the lung was so compressed and diseased that the division of the upper and lower lobes was lost and the lung fused with the mediastinal tissues. Secondly, the mediastinal glands (Fig. 4) were enlarged, completely caseous and fused together by hyaline thickened capsules. The left pulmonary artery was surrounded and compressed by these

glands so as to show only a slitlike opening. The central part of the lung showed advanced tuberculous pneumonia (caseation), and in the center of this was a triangular cavity measuring 2 by 3 cm. (Fig. 4) with its base at the pleural surface and its apex communicating with a bronchus (Fig. 4). The apex of the lung and a small triangular area at the base were atelectatic and showed only a few pin point caseous spots.

A brief description of the remaining organs will suffice. The right lung was free in the right thorax, which contained approximately 2 c.c. of serous fluid. The apex and anterior margin showed slight emphysema, but the lung as a whole was somewhat compressed. There were a number of small nodular masses which showed through the pleura as slightly raised yellow elevations which varied in diameter from 1 to 5 mm. On section, these nodules were

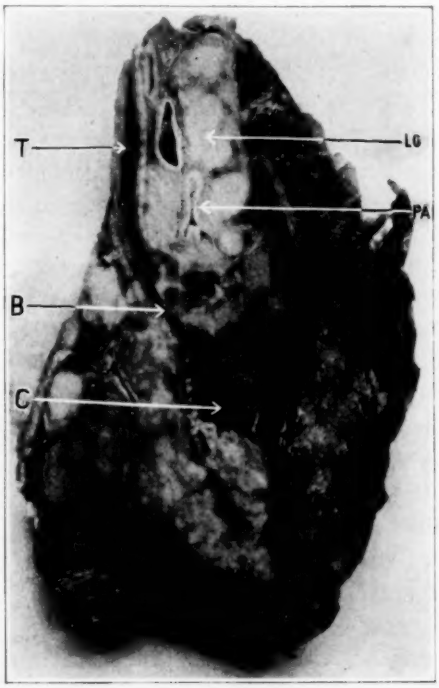

Fig. 4.—Direct communication of trachea (*T*) with cavity (*C*). Caseous and fused mediastinal lymph glands (*LG*). Compressed left pulmonary artery (*PA*). Point at which microscopic section taken (*B*).

caseous throughout and the center of the upper lobe showed more recent miliary conglomerates.

The brain showed no microscopic tubercles, but the meninges were edematous at the base and were gelatinous. The peritoneum and abdominal organs were without gross lesions. The intestine and mesenteric lymph glands were very carefully examined for a possible primary focus, but no evidences of any infection were discovered.

The microscopic lesions were very typical and of especial interest as they bear on the probable sequence of events. The mediastinal glands revealed complete replacement by cheesy caseous material and fused with the surrounding hyaline fibrous tissues. A section, taken through the bronchus lead-

ing to the cavity and the surrounding tissue at the pointed marked B (Fig. 4) showed a well marked proliferation and desquamation of the lining epithelium of the bronchus with exuded serum and mononuclear cells. The submucosa was very vascular and infiltrated with similar inflammatory cells. The epithelium of the bronchial glands showed disintegration. In close proximity to the bronchus were two small peribronchial lymph glands. These showed central caseation surrounded by an epithelioid celled zone and giant cells, but separated from the bronchus and each other by granulation tissue, rich in large pale mononuclear cells.

Sections of the brain through the sylvian fissure and middle cerebral artery showed a very marked lymphocytic infiltration following the course of the vessel. There was however, no fixed tissue reaction either in the form of endothelial proliferation or formation of definite tubercles.

In the liver and spleen were scattered minute tubercles consisting of epithelioid cells and an occasional giant cell, without caseation.

COMMENT

In reviewing this case from the clinical standpoint, several facts stand out in bold relief. The close association with the father, who was suffering from open tuberculosis, was the evident reason for the early infection of the patient. As to the mode of entry of infection one cannot dogmatize. However, the necropsy findings showed no evidence of tuberculosis of the alimentary tract. In this connection the possibility of infection by this route, with passage into the lymphatics and general circulation without causing a local lesion, must be considered. Another possibility is that the otitis media was of a tuberculous nature. There is no proof for or against this. The obvious and, therefore, attractive theory is that inhalation of droplets or dust carrying the tubercle bacilli resulted in a tracheobronchial lymph node infection by way of the pulmonary road. In favor of this is the history of a persistent cough from the age of 3 months, and the presence of shadows at the hilum in the roentgen ray. These at such an early age are suggestive of tuberculosis. Finally, and what seems of most importance, a definite shadow (Fig. 1) in the middle part of the left lung, which later was proved to be the center of the tuberculous lesion.

As to the diagnosis, we would like to emphasize the importance of the history of exposure, which should always lead one to search carefully for signs of tuberculosis. When first seen, it was impossible to make a diagnosis by physical examination alone. Here the obvious value of the tuberculin test and the roentgen-ray examination is apparent. The first tuberculin test was doubtful, but on being repeated gave a definitely positive reaction. The intradermal method was used, being much more reliable than the Pirquet cutaneous method. A positive test at this age always means active tuberculosis. The roentgenogram of the chest showed definite signs of enlarged glands at the hilum and of parenchymal consolidation as well. This, in the presence of a

positive tuberculin reaction, made the diagnosis quite certain. Without these two aids the diagnosis would have been impossible until much later in the course of the disease.

The prognosis in tuberculosis when infection has taken place in the first three months is practically always fatal, and either a miliary tuberculosis, a tuberculous meningitis, or more rarely a tuberculous bronchopneumonia may follow the original infection.

It was possible by the roentgen ray to diagnose the anatomic lesion of the lungs with great accuracy. The tuberculous adhesions attaching the lung to the parietal pleura and preventing complete collapse of the lung are well shown and, as previously noted, were confirmed at necropsy. It would also appear that the portion of the lung, which showed the first sign of disease by the roentgen ray, was the place at which the caseous mass broke through into the pleural cavity. The roentgen ray also showed a definite thickening of the left pleura which was confirmed at necropsy.

It is of interest to note that during the last illness of the patient there was no fever. This may occur in overwhelming infections with tuberculosis.

The pathologic findings, both gross and microscopic, confirm the clinical in nearly every respect. It seems to us that all the evidence points to the following sequence of events: Infection of the respiratory tract by direct contact, passing of the bacilli into lymph channels and spaces of the peritracheal or peribronchial tissues and involvement of the peribronchial and peritracheal lymph glands. The complete destruction of these glands and the degree of caseation point to these as the oldest lesions in the thorax. In the absence of any anatomic evidence in the intestine or mesenteric lymph glands, it would seem permissible to question seriously or even rule out the intestinal route.

It would seem that there is probably a relation between the marked involvement of the greater part of the central portion of the left lung and the compression of the main branches of the pulmonary artery (Fig. 4), which supply this area. There are two possibilities, either a direct invasion of the wall of one of the branches of the artery or a rupture into a corresponding bronchus. Either event would throw bacilli into a part of the lung in which the resistance was lowered by interference with the circulation. That the lung lesion was at first localized to such an area is, we think, well shown by the roentgenogram (Fig. 2). Then followed caseation with extension of the lesion and cavity formation. The direct connection of the cavity with a larger bronchus allowed aspiration of infected material into the right lung. The very recent lesions in the meninges, liver and spleen may be considered due to a terminal invasion of the greater circulation.

HEALTH AND GROWTH OF CHILDREN IN AN INSTITUTION *

S. E. KATZ, M.S., AND HORACE GRAY, M.D.
BOSTON

"Children in an institution can be kept in much better condition than in most private homes." [1] This contradiction to the prevalent impression, and tribute to institutional possibilities, has been illuminating to us, as we have been engaged for six months in a somewhat similar study. This study differs in certain particulars, which will be recited below, but mainly in two: (1) It concerns children of the very poorest classes, namely, of parents who were either unable to support them, or who were dead, and (2) it investigates not only the physical status, but also the anthropologic and mental. The present paper in a large degree confirms Holt and Fales' [1] surprising but important findings, and considers certain further points of interest in connection with institutional children.

THE INSTITUTION

The institution is a Home for Jewish Children, receiving them from a child caring agency. The house is a brick building of three stories, with plenty of air space and ventilation. Its situation is in a big Jewish community on an elevation at the outskirts of Boston, facing a park. There is a dormitory for each of the following four groups, older and younger boys, older and younger girls. These dormitories are located on the second and third stories with bathing facilities adjacent; the dining room and offices are on the ground floor; and in the basement are shower baths and wash basins which the children use after play hours. The playground consists of a big yard in the rear of the building enclosed by a high brick wall, and is furnished with an adequate amount of apparatus of which the children make frequent use. During the summer months, the older children are usually sent for a fortnight to the country, where a camp is maintained by the institution.

INMATES

Contrary to Holt and Fales' subjects, practically all of these children come from the very poorest class; most of them are orphans, some half orphans, only a few have both parents. The race is, of course, Jewish. Nearly all are native born, while their parents were

* Received for publication, Jan. 23, 1924.

1. Holt, L. E., and Fales, H. L.: Observations on the Health and Growth of Children in an Institution, Am. J. Dis. Child. **26**:1 (July) 1923.

practically all foreign born. Most of the children have been raised in the city. At first observation the children appear to be in good physical condition, with very few exceptions, and furthermore, happy and gay, not suffering in the least from institutional repression.

The ages of the children range from 5 to 17 years, though there are very few below the age of 6 or above the age of 16.

The length of stay, as one would naturally expect for children of this destitute class, is rather long. The girls show a longer residence than the boys. The average is 4.3 years. The mode (commonest stay) corresponds. Twenty-five per cent. have been in the institution for five years, or more, and only a very small percentage have a residence of less than one year (Table 1).

TABLE 1.—*Years of Residence*

	Less Than 1 Yr.	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	Totals
Boys, number.....	14	14	17	12	20	6	6	4	3	1	0	0	97
Girls, number.....	6	8	9	10	7	4	5	3	0	3	3	1	59
Both sexes, number.....	20	22	26	22	27	10	11	7	3	4	3	1	156
Percentage.....	13	14	17	14	17	6	7	4	2	3	3	0.8	98.8

The number of families represented in the institution was eighty-one. The size of family from which the children came is shown in Table 2. The mode is 4, the average 4.6 children. This point is of interest because it shows that the families are smaller than is usually believed to be the case in this class.

TABLE 2.—*Size of Family*

	Number of Children in Family										Not Ascertained	Total
	1	2	3	4	5	6	7	8	9	10		
No. of instances of each....	4	9	26	37	26	17	13	8	0	2	14	156

The distribution of siblings actually in the institution is seen in Table 3. The mode is one and the average is 1.93.

TABLE 3.—*Distribution of Siblings*

	Number of Siblings						
	1	2	3	4	5	6	Total
Number of such instances.....	37	22	16	4	1	1	156

GENERAL HEALTH

On application for admission, a complete physical and mental examination is usually given by the physician of the child caring agency, to exclude children who are defective or acutely ill. Malnutrition, however, is not a cause for exclusion, but rather for admission. There

is no quarantine regulation for children admitted. The institution has a small hospital, where children who become ill are separated and cared for by the resident nurse. She also attends to all minor ailments or slight injuries. The more serious ones are seen by the visiting physician who gives the children a general physical examination once a year. No epidemic of any sort has occurred for a number of years, and deaths are rare. During the last year there were few cases of serious illness; any such case is immediately removed to one of the city hospitals.

The good health of the children is probably the result of the regular life. The prevalent impression that children living in an institution decline in vitality, and that their development is inhibited, would be greatly modified by visiting an institution of this sort. Observation of

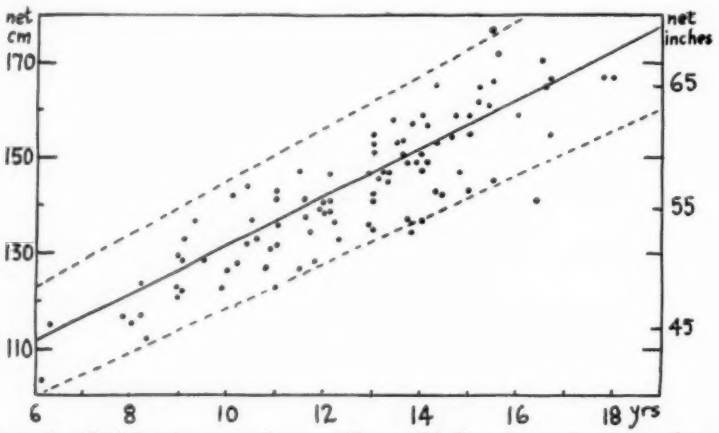

Chart 1.—Height for age, boys. The solid line in each chart shows the standard height, and the dotted line shows the zone 10 per cent. below and above the standard height.

these children would lead to the belief that institutional life may just as well accelerate growth. As Holt and Fales state: "The carefully controlled life in any properly managed institution, the regular hours, the good food and the lessened chances of infection, make it possible to keep children in institutions in excellent health, in fact in much better condition than they could be kept in most private homes," especially where the sanitary conditions in the Ghettos of the big Jewish centers in the East leave much to be desired. Except at the public school, our children do not come in contact with others.

ROUTINE

The regimen, although strict, is liberal enough not to interfere with the activity of normal children. They rise at 6 a. m., have about a half hour to attend to their toilet, and then attend a short service.

At 7 they have breakfast. In the dining room they have more liberty than in many institutions; they are allowed to talk and even to move about somewhat. A prayer is offered at the beginning and the end of each meal, and for a few seconds before the prayer, no talking is allowed. About thirty minutes are given to each meal.

After breakfast the children make up their own beds. From 9 a. m. to 12 m. they attend the neighboring public school. At 12:30 dinner is served, after which they return to school for a while. At the Home again at 3 p. m. the older boys have manual training (printing, carpentry, machine work) and the girls domestic science. Both also have Hebrew classes. The younger children have this time for play. No systematic physical education is provided at present. Supper is served at 5:30 p. m. Evenings are spent partly in studies, somewhat supervised, and partly at play. The younger children go to bed at 7 p. m.,

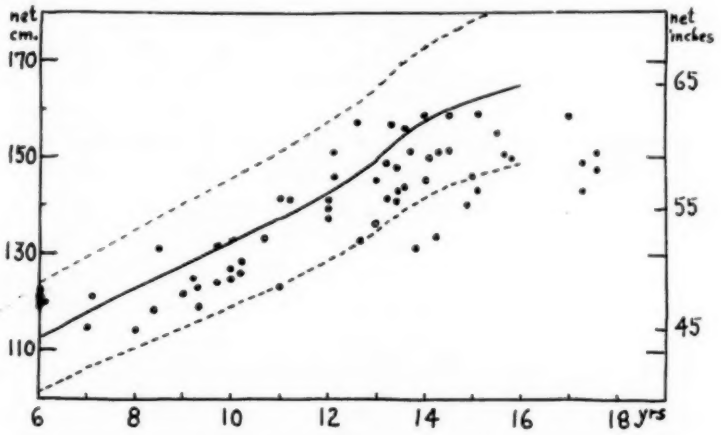

Chart 2.—Height for age, girls.

the older ones at 9. Children must take showers at least twice a week. Special emphasis is laid on oral hygiene, tooth brush and paste being expected to be used twice a day.

During July and August the rising hour is changed to 7 a. m., and breakfast is at 8. The morning period from 9 to 12 is spent at manual training or Hebrew classes, the afternoons and evenings are given over to play. At frequent intervals the children are taken out to the beaches or other places for recreation.

The institution takes special pride in its Boy Scouts and Camp Fire Girls, to which the older children belong. The summer camp is conducted by these organizations. The children are also encouraged to participate in various sports. They have a basketball team in the winter and a baseball team in the summer time. Competition for membership on these teams is keen.

DIET

The meals are plentiful and consist of the food usually served in Jewish homes. Breakfast consists of cereal, fruit, cocoa and bread and butter; dinner consists of soup, meat and a vegetable, bread, some sort of pudding and water; supper consists of milk soup, jelly and bread and butter with either cooked or uncooked fruit as dessert. Eggs and fish are often substituted for soup.

The food is served on big platters, one platter for a table. At the head of the table sits an older child who serves the five or eight children at his table. No attempt has been made to determine the caloric consumption, as this was impractical under the present dining room arrangement. The general appearance of the children is a sufficient index of the quality and quantity of the food consumed.

OBSERVATIONS ON GROWTH

As stated before, this report deals only with one phase of the investigation, namely, physical development. The subjects numbered ninety-seven boys and fifty-nine girls. Measurements were recorded in metric units. The weights were taken on a Fairbanks scale that had been checked before using. The scale reads to ¼ of a pound, and the readings were computed to tenths of kilograms. Shoes, coats, and contents of pockets were removed. The clothing (July) we found, like Holt and Fales, to average only 0.7 kg. (about 1½ pounds) while for the younger boys and girls it weighed somewhat less. Deductions have been made so that all measurements here reported are net. All the weighing was done between 10 and 12 in the morning; that is, from two to four hours after eating.

The height was taken as follows: The children removed their shoes and stood with head, heels and sacrum snugly against the wall. A light triangular piece of cardboard was brought down until it touched the vertex firmly, and the reading was then taken to the nearest millimeter. It was found that the error of two successive measurements was not greater than 2 mm.; this was owing to a change in position that a child may assume, and was found to be still further reducible by taking the measurements quickly. Stem length was also measured.[2] It is planned to take these measurements once a month to determine rate of growth and seasonal variations. The present paper deals only with the data found during the month of July at our first series of observations. These data have been analyzed for the relation of weight to height and height to age, relation of nutrition to birth, length of residence, size of family, tuberculous history of parents.

---

2. Gray, Horace: Sitting-Height and Stem-Length in Private School Boys, Am. J. Dis. Child. **23**:406 (May) 1922.

TABLE 4.—*Developmental Status—Relation of Height and Age*

	Percentage of Population			
	Above Average	1-10% Below Average	11% or more Below Average	Total
Boys	37	60	3	100
Girls	20	65	15	100
Both sexes	31	61	8	100

Age and Height Relation.—We noticed that the children were of rather low stature, for they exhibited a larger percentage of below average in height than the children studied by Holt and Fales.[1] This may be owing to either their racial difference or to the poorer economic status. Charts 1 and 2 show the height and age relationship in graph form. The solid line shows the standard height for age and is based on the values given by Holt and Howland.[3] The dotted lines in each chart mark the zone, including the height of boys and girls respectively, 10 per cent. below and 10 per cent. above the standard height for age (nearest birthday) as in Holt and Fales' article.

TABLE 5.—*The State of Nutrition, with Relation of Weight to Height*

	Percentage of Population			
	Above Average	Tolerable, i. e., 1-10% Below Average	11% or more Below Average	Total
Boys	71	26	3	100
Girls	76	22	2	100
Both sexes	73	24	3	100

Weight and Height Relation.—This relationship has been found by various observers to be a most reliable index of nutrition. As shown in Table 5, these children show a large percentage above the average: 71 per cent. of the boys and 76 per cent. of the girls are in that group, and only 3 per cent. of the boys and 2 per cent. of the girls are 11 per cent. or more below average. It is of interest to note that the five children who are in the last group have been in the institution for less than six months.

Charts 3 and 4 show the distribution of weight for height for the boys and girls, respectively.

Relation of Length of Residence to State of Nutrition.—Twenty children who were in the institution less than 1 year were compared with eighteen children resident 7 years or more. The very marked improvement is shown in Table 6. Although the numbers are small, the difference is so striking that it seems worth noting. Whereas, in the first group the tolerable zone of normality contained 45 per cent. of the children, in the second group it fell to only 17 per cent.

3. Holt, L. E., and Howland, J.: Diseases of Infancy and Children, Ed. 8, New York, D. Appleton & Co., 1922, p. 23.

TABLE 6.—*State of Nutrition Improved Strikingly by Residence in the Home*

	Above Average	1-10% Below Average	11% or More Below Average
Less than one year: Number	11	8	1
Percentage	55	45	5
Seven years or more: Number	15	3	0
Percentage	83	17	0

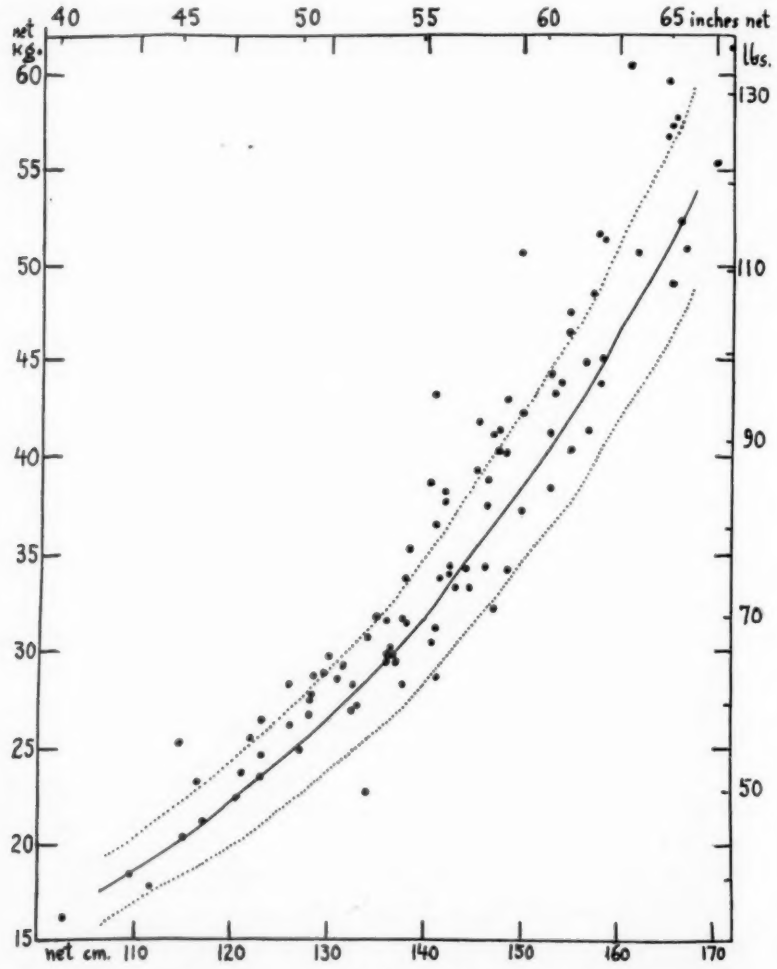

Chart 3.—The distribution of weight for height for ninety-seven boys.

Relation of Parental Tuberculosis to Nutrition of Offspring.—Thirty-five children gave a positive family history for tuberculosis in either one or both parents. The data are represented in Table 7, and are seen to compare badly with Table 5 for all the inmates of the home. Notice the figures in the bottom line of each table.

TABLE 7.—*State of Nutrition Worse in Children of Tuberculous Parents*

	Above Average	1-10% Below Average	11% or More Below Average
Number	13	20	2
Percentage	37	57	6

Relation of Size of Family to Nutrition.—We arbitrarily divided our inmates into two groups: four children or less in one group and five or more into a second group, and compared the state of nutrition of the children in these two groups. The data in Table 8 are negative, i. e., the state of nutrition did not suffer by an increase in the size of the family.

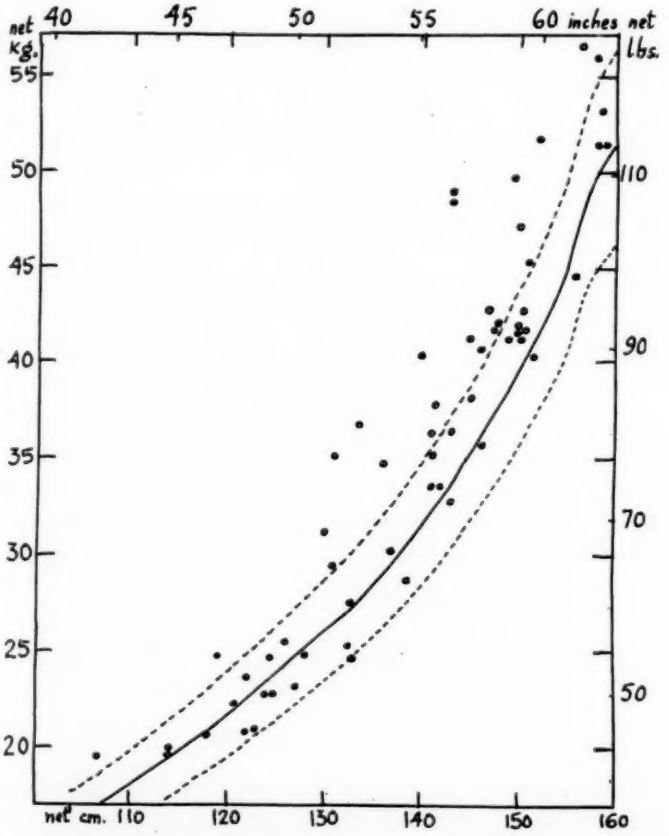

Chart 4.—The distribution of weight for height for fifty-nine girls.

TABLE 8.—*Relation of Size of Family to Nutrition*

	Above Average	1-10% Below Average	11% or More Below Average
Four or less children in family: Number	45	24	5
Percentage	61	32	7
Five or more children in family: Number	38	25	3
Percentage	57	38	5

Relation of Order of Progeny to Nutrition.—There were twenty-seven first-born children. We compared this group with twenty-four children that were either fifth-born or more. The data are given in Table 9. The first-born were more frequently above normal. This finding is contrary to some statements in the literature.

TABLE 9.—*Relation of Order of Progeny to Nutrition*

	Above Average	1-10% Below Average	11% or More Below Average
First-born: Number	18	7	2
Percentage	67	26	7
Fifth or more born: Number	13	11	0
Percentage	54	46	0

SUMMARY

1. Children of the poorest class, when under proper institutional care, are shown to catch up rapidly to normal children in physical respects. Whether they do so in the intellectual sphere will be dealt with in another paper.

2. The one hundred and fifty-six children studied were generally undersized. Whether that is due to a racial difference or to a retarded development could not be determined.

3. The children studied were in a very good state of nutrition; only 3 per cent. were found to be 11 per cent. or more underweight.

4. The longer they stayed in the institution the larger was the percentage of children who were above the average in nutrition and development.

5. The children found to be in better health were those with no history of parental tuberculosis, and the first-born children. On the other hand, their nutrition did not suffer by an abundance of brothers and sisters.

A MORPHOLOGIC AND QUANTITATIVE STUDY OF THE BLOOD CORPUSCLES IN THE NEW-BORN PERIOD*

HYMAN SHALIT LIPPMAN, M.D., PH.D.
MINNEAPOLIS

The condition of the blood in the new-born has been studied by numerous investigators since Denis[1] published the first observations on the subject in 1831. In many instances there has been insufficient data to warrant the conclusions submitted. Statistical results, to be of any great value, must be based on a reasonably large group of cases preferably with repeated observations, and this factor apparently has been disregarded in most of the work published on the blood of the new-born.

In practically every case the blood has been studied at twenty-four hour intervals, usually for the first week and occasionally through the first month. Sometimes the first day has been divided into two or three parts in order to follow the changing blood picture of the first twenty-four hours.

A study of the literature on this subject shows that, though very marked changes occur during the first forty-eight hours after birth, little effort has been made to determine the exact times at which the important modifications take place.

At the suggestion of Dr. R. E. Scammon, the present study has been based chiefly on the blood of the new-born during the first forty-eight hours after birth, dividing this interval into nine parts.

The study of the finer structure of the leukocytes during the first few days of life has received less consideration than cell counts and hemoglobin determinations. The fluctuating white blood count during this period promised interesting changes in the morphology of the blood. In this work, therefore, the structural changes in the leukocytes have received primary consideration.

SUMMARY OF LITERATURE

The greater part of the literature, previously published, on the morphology of the blood of the new-born is given here in outline form. There are a few facts, however, that cannot be presented in such an outline and these are briefly discussed below.

---

* Received for publication, February 27, 1924.

* From the Department of Anatomy and the Department of Pediatrics, the Medical School, University of Minnesota.

1. Denis: quoted by Bayer.

TABLE 1.—*Summary of Published Data on the Morphology of the Blood of the New-Born*

Aitkin, J.: J. Obst. & Gynec. Brit. Emp. **1**: 414, 1902
Hemoglobin.—106 per cent., birth average
Red Blood Cells (count in millions).—Birth, 6.13; 1st hour, 6.45; 12-24 hours, 7.67; 48 hours, 8.35; 3 days, 7.68; 5 days, 6.75; 7-10 days, 5.89
Leukocyte Count.—2-16 hours, taken before feeding, 18,525; 2d day, after feeding, 22,800; 3d day, 15,585; relation to meals not noted
Differential.—Erythroblasts present in all cases directly after birth; present at 48 hours in 24 of 25 smears; present at 5-9 days in 15 of 27 smears; R. B. C. 3¼-10¼ microns in diameter; 14 cases at birth: lymphocytes, 46-66 per cent.; polymorphonuclears, 27-46 per cent.
Remarks.—Amount of hemoglobin does not vary with number of red blood cells. Increase in leukocyte count after meals average 10,000 per cu. mm.

Takasu, K.: Arch. f. Kinderh. **39**: 346, 1904
Hemoglobin.—130.2 per cent. first 3 days
Red Blood Cells (count in millions).—Average first three days, 4.84
Leukocyte Count.—First 3 days, 13,000 to 28,000; 4-10 days, 14,700 average
Differential.—Nucleated red blood cells in nearly all cases; eosinophils in the new-born vary from 0 to 9.6 per cent.; average from 2 hours to 10 days, 2.8 per cent.
Remarks.—Japanese children show racial peculiarity of high hemoglobin

Perlin: Jahrb. f. Kinderh. **58**: 549, 1903
Hemoglobin.—116-119 per cent. until fourth day
Red Blood Cells (count in millions).—1st day, 5.71; 2d day, 6.23; 3d day, 6.29; 4th day, 6.14; 5th day, 5.67; begins to drop at 11 days
Leukocyte Count.—17,146, 1st day; 17,857, 2d day; 16,281, 3d day; 16,960, 4th day; 14,450, 5th day

Karnitzki, A.: Arch. f. Kinder. **36**: 42, 1904
Hemoglobin.—12.7 gm. per hundred cubic centimeters of blood
Leukocyte Count.—16,000, 1st day; 16,000, 2d day; 15,300, 3d day
Differential.—Studied 1,000-1,500 cells in his differentials; polymorphonuclears are larger, thicker and richer in chromatin early in life; neutrophils difficult to distinguish from eosinophils in some smears; believes the eosinophil granules come from the neutrophil nucleus; several degeneration forms noted in infancy
Remarks.—Hemoglobin does not vary with red cell count

Krüger: Arch. f. path. Anat. **106**: 1, 1886
Remarks.—Hemoglobin of mother equal to that of new-born; after a few days the hemoglobin of infant is higher

Carstanjen, M.: Jahrb. f. Kinderh. **52**: 215, 333, 1900
Hemoglobin.—113 per cent., birth average
Differential.—Polymorphonuclears: 1st day, 73.45 per cent.; 3d day, 66.18 per cent.; 6th day, 41.81 per cent.; 9th day, 36.12 per cent. Lymphocytes: 1st day, 16.05 per cent.; 3d day, 18.84 per cent.; 6th day, 35.11 per cent.; 9th day, 41.86 per cent. Transitionals: 1st day, 8.43 per cent.; 3d day, 11.11 per cent.; 6th day, 17.52 per cent.; 9th day, 18.66 per cent. Mononuclears: 1st day, 0.17 per cent.; 3d day, 0.14 per cent.; 6th day, 0.75 per cent.; 9th day, 0.66 per cent. Eosinophils: 1st day, 1.9 per cent. During first day average nucleated red blood cells equaled 1.3 per 100 leukocytes. First 24 hours polymorphonuclears are highest; polymorphonuclears equal lymphocytes at 6-9 days
Remarks.—Studied only five cases

Elder, G., and Hutchison, R.: Edinburgh M. J. **41**: 105, 1895
Hemoglobin.—95-115 per cent., birth average
Leukocyte Count.—Birth average, 17,884
Differential.—5-12 erythroblasts per 100 leukocytes at birth; no basophils found
Remarks.—No more anisocytosis than in adult blood. Studied small number of new-borns

Williamson, C. S.: Arch. Int. Med. **18**: 505 (Oct.) 1916
Hemoglobin (grams per 100 c.c. blood).—1st day, 23.25; 2d day, 22.78; 3d day, 22.78; 4th to 8th day, 22.12
Remarks.—Hemoglobin findings agree with those of Leichtenstern

Schiff, E.: Jahrb. f. Kinderh. **34**: 159, 1892

Hemoglobin.—	1st day	2d day	3d day	4th day	5th day
Prague	104.6%	104.2%	100.1%	96.5%	94.0%
Budapest	144.0	135.0	135.0	130.0	132.3

Remarks.—Quoted by Von Reuss; indicates racial differences in hemoglobin

Fehrsen, A. O. M.: J. Physiol. **30**: 322, 1903
Hemoglobin.—Birth average, 102-125 per cent.; average fall in first few days, 10 per cent.
Red Blood Cells (count in millions).—First 24 hours, 4.30 to 7.25
Leukocyte Count.—Highest value up to 20 hours, 22,500; lowest, 7,600
Differential.—Erythroblasts always present first 2 hours, never after 13 hours; when the leukocyte count is 18,000+, there is an increase in polymorphonuclears

TABLE 1.—*Summary of Published Data on the Morphology of the Blood of of the New-Born.—(Continued)*

Heimann, F.: Ztschr. f. Geburtsh. u. Gynäk. **69**: 165, 1911
Hemoglobin.—Reduced in icterus neonatorum; the reduction is proportional to the degree of jaundice. Average mild icterus, 102 per cent.; average moderate icterus, 101 per cent.; average marked icterus, 93 per cent.; average control, 113 per cent.
Red Blood Cells.—Decrease in icterus neonatorum
Leukocyte Count.—No marked difference between normal and icterus neonatorum
Differential.—Erythroblasts more common in icterus neonatorum; no polychromophilia noted; eosinophils are reduced 50 per cent. in icterus neonatorum
Remarks.—Fifty cases of icterus neonatorum were studied and compared with 50 normal new-borns

Lucas, W. P.; Bradford, F. D.; Hoobler, H. R.; Cox, A.; Jones, M. R., and Smyth, F. S.: Am. J. Dis. Child. **22**: 525 (Dec.) 1921
Hemoglobin.—1st day, 124 per cent.; 2d day, 122 per cent.; 3d day, 114 per cent.; 4th day, 119 per cent.; 5th day, 112 per cent.
Red Blood Cells (count in millions).—1st day, 5.51; 2d day, 5.35; 3d day, 5.11; 4th day, 5.24; 5th day, 4.98
Platelet Count.—1st day, 305,000; 2d day, 300,000; 3d day, 308,000; 4th day, 310,000; 5th day, 295,000; lowest count, 196,000
Leukocyte Count.—1st day, 19,200; 2d day, 15,300; 3d day, 11,100; 4th day, 10,300; 5th day, 10,900
Differential.—Nucleated red blood cells present in 52 per cent. of cases on first day (1 per 100 leukocytes); 5 per cent. of cases on second day (½ per 100 leukocytes); fine basophilic granules in red blood cells first day, rarely after this

Differential Count:	1st day	2d day	3d day	4th day	5th day
Polymorphonuclears	70	62	58	54	49
Lymphocytes	20	24	27	30	34
Transitionals and Mononuclears	9	11	12	13	15
Eosinophils	1	1	1	1½	3

Remarks.—Hemoglobin in severe icterus neonatorum equal to normal; no reduction in red cell count in icterus

Barbosa, J. M.: Oporto, 1921
Hemoglobin.—1st day average, 160 per cent.; 2d day average, 142 per cent.; 1st 20 days average (males), 146 per cent., (females) 139 per cent.
Red Blood Cells (count in millions).—1st day, 6.34; 2d day, 6.15; 1st 20 days, average (males), 6.56, (females) 5.92
Leukocyte Count.—1st day, 20,581; 2d day, 14,802; 5th day, 13,301; average 20 days, (males) 14,039, (females) 15,104
Differential.—Lymphocytes equal to polymorphonuclears on the fifth day

	Days	Polymorpho-nuclears	Lympho-cytes	Eosino-phils
8 cases	1	74	20	1½
4 cases	2	59	24	4
	3	62	23	3½
	4	53	30	3
6 cases	5	47	37	4½

Remarks.—Studied the blood of Portuguese new-borns

Bayer, A.: Diss. Bern. 1881
Red Blood Cells (count in millions).—5 minutes to ¾ hour, 4.41; 3½ hours, 5.43; 1 day, 5.11; 2 days, 4.92; 3 days, 5.12
Leukocyte Count.—¾ hour to 16 days: minimum, 5,700; maximum, 25,000; number of cases not stated
Remarks.—Includes prematures

Slawik, Ernst; Ztschr. f. Kinderh. **25**: 212 (June) 1920
Platelet Count.—Average to 10 days, 320,000; one case, 65,000; highest, 4-6 days
Leukocyte Count.—Polymorphonuclear leukocytosis first few days; lymphocytes appear in excess on fifth or sixth day
Differential.—First day marked anisocytosis of platelets, 1 micron to size of red blood cells; first few days, 50-60 per cent. are medium sized, the remainder mostly larger; after 2 weeks the smaller platelets are in excess; birth average, 6 nucleated red blood cells per 100 leukocytes; present in 14 of 25 cases in second week

Biffi and Galli: Riv. di Clin. Pediat. **1**: 1, 1908
Red Blood Cells (count in millions).—Average 2d day, 7.00
Differential.—In 28 of 29 cases, nucleated red blood cells were present

Gundobin, N.: Jahrb. f. Kinderh. **35**: 187, 1893
Red Blood Cells (count in millions).—6.70 average first few days
Differential.—Leukocytosis at birth due to over ripe elements; on the second day this is less

Woino-Oranski: Quoted by Fehrsen
Red Blood Cells (count in millions).—8.30 average first few days
Leukocyte Count.—Birth average, 16,980; 20 hours, 20,980; 2d day, 25,580

Schiff, Ernst: Jahrb. f. Kinderh. **34**: 159, 1892
Red Blood Cells (count in millions).—1st day, 6.00; 12th day, 6.00

TABLE 1.—*Summary of Published Data on the Morphology of the Blood of of the New-Born.—(Continued)*

Viereck, H.: abstr. Folia. haematol. **1** :36, 1904
Red Blood Cells.—Count in new-born male 4 millions greater than new-born female

Mayers, L. H.: Arch. Int. Med. **30**: 478 (Oct. 7) 1922
Red Blood Cells (count in millions).—Birth average, 7.63
Remarks.—No direct relationship between red blood cells and amount of hemoglobin

Drinker, Cecil: Oxford Med. **2**: 509, 1920
Differential.—Naked red blood cell nuclei found only in cases of active proliferation of red-forming marrow tissue; same applies to megaloblasts

Cadet: Quoted by Slawik
Red Blood Cells (count in millions).—1st day, 171,000; 8th day, 350,000; gradual rise from 1st to 8th day

Rebaudi: Quoted by Lehndorff
Platelets.—Birth average, 95,000

Morse, M.: Boston M. & Surg. J. **166**: 448, 1912
Platelets.—Birth, 100,000 to 412,000; increase in icterus neonatorum
Remarks.—If platelet count at birth is high, it decreases during first week; if low at birth, it increases in first week

Hess and Syderhelm: Abstr. Fol. Haem. Zentral. Organ **18**: 112, 1916
Leukocyte Count.—During crying the count increases, often 8,000 per cu. mm.; increase is due to lymphocytes

Fischl, R.: Arch. f. Kinderh. **15**: 470, 1892
Differential.—No eosinophils seen until 7th fetal month; eosinophils in the new-born vary from 0.73 to 8.6 per cent.; average 4.13 per cent. nucleated red blood cells

Warfield, L. N.: Am. Med. **12**: 457, 1902
Leukocyte Count.—Nucleated red blood cells disappear rapidly first 3 days; the polymorphonuclears are relatively and absolutely increased in number shortly after birth
Differential.—Eosinophils vary from 0.2 to 6.0 per cent., average 1.8 per cent. in new-born; myelocytes and mast cells are rare. The lymphocytes do not equal polymorphonuclears in number until the 11th day

Arneth, J.: Arch. f. Gynaek. **74**: 145, 1905
Differential.—A large percentage of the neutrophils are single lobed in the first day: in one case 60 per cent. were single lobed; at 7-8 days, 3, 4 and 5 lobed nuclei are more common, while single lobed nuclei are very uncommon; from the first to the seventh day there is a constant transition from one picture to the other
Remarks.—These findings are checked by Dupérié and Kadisson (quoted by Bayer)

Frank, M.: Ztschr. f. Kinderh. **31**: 16 (Nov.) 1921
Differential.—Change from a myeloid to a lymphoid type of blood usually occurs on third or fourth day; though it may occur at thirty-six hours; agrees with Arneth in his result; nothing characteristic in the eosinophil curve; basophils scarce; during the first few days the small lymphocytes are more numerous than the large; in some cases 25 per cent. of the leukocytes were small lymphocytes; azure granules are few and often are entirely absent in new-born blood; in the next few days they become more numerous; the small lymphocytes contain few azure granules whereas the large lymphocytes with pale poorly stained cytoplasm contain many; this is an indication that azure granules in excess denote cell aging

Light, C. A.: New York M. J. **74**: 1000, 1901
Leukocyte Count.—The increase in the white count is early and remains present during the entire first two years

Scipiades, E.: Arch. f. Gynaek. **70**: 630, 1903
Red Blood Cells.—Drop in red count first day and secondary rise on third day
Leukocyte Count.—Highest on first day count; drops in 2-3 days; secondary rise occurs on seventh day, when the cord separates

Demme: Quoted by Bayer
Leukocyte Count.—First 72 hours breast fed; 1 white blood cell for each 135 red blood cells; artificially fed cases show 1 white blood cell for each 122 red blood cells

1. *The Hemoglobin.*—The work done on the hemoglobin determination in the new-born period shows that the values are higher at this time than at any other period in the child's life. The results of Takasu [2] and

2: Takasu, K.: Blutuntersuchungen bei den japanischen Kindern. Arch. f. Kinderh. **39**: 346, 1904.

Schiff [3] tend to show that the amount of hemoglobin varies in different races.

2. *The Red Blood Cells.*—Soon after birth there is a rise in the red blood cell count lasting for different time intervals, according to various observers. This rise is followed by a fall in the number, often below the count at birth.

Engelsen [4] was one of the first who noted that there was an increase in the diameter of the red blood cells of the new-born.

Silbermann,[5] one of the pioneers in the study of new-born blood, observed many shadows in the red blood cells due to a lack of hemoglobin. He quotes Ponfeck,[6] who first observed this change. Ponfeck noted that these cells were more numerous in disturbances of the newborn, and that occasionally poikilocytosis could be seen in the new-born's blood.

Hoffmeier [7] is quoted by Silbermann as having first shown that the red blood cells of the new-born did not tend to form in rouleaux.

According to Vierordt,[8] Neumann [9] was one of the first to find nucleated red blood cells in the new-born's blood. Neumann noted that this blood often contained cells which resembled those seen in leukemia.

The majority of those who have studied the new-born blood have found nucleated red blood cells present during the first few days.

Fischl [10] did not find many erythroblasts in new-born blood. On the contrary, he claims that their presence is exceptional. He found them usually in premature children. He further found that the rouleaux formation was normal. Karnitzki,[11] on the other hand, found nucleated red blood cells in the normal nursling seven and one-half months after birth, but no other investigator has noted this in the normal infant.

---

3. Schiff, Ernst: Neure Beiträge zur Haemotologie der Neugeborenen mit besonderer Rüchsicht auf die Abnabelungzeit, Jahrb. f. Kinderh. **34**:159, 1892.

4. Engelsen, E.: Undersögelser over Blodlegemernes Antal, Hämoglobinmengde og Storrelse. Afhandl. for Doktorgraden: Medicin. Kopenhagen, abstr. Jahresb. ü. d. Leistung. in d. ges. Med. **1**:127, 1884.

5. Silbermann, O.: Zur Hämatologie der neugeborenen, Jahrb. f. Kinderh. **26**:252, 1887.

6. Ponfeck: quoted by Silbermann, Footnote 5.

7. Hoffmeier: quoted by Silbermann, Footnote 5.

8. Vierordt, H.: Physiologie des Kindersalters, Gerhardt's Handbuch d. Kinderh. **1**:53, 1877.

9. Neumann: quoted by Vierordt, Footnote 8.

10. Fischl, R.: Zur Histologie des kindlichen Blutes, Arch. f. Kinderh. **15**: 470, 1892.

11. Karnitzki, A.: Ueber das Blut gesunder Kinder, Arch. f. Kinderh. **36**: 42, 1904.

Geissler and Japha,[12] Hayem,[13] and Loos [14] conclude that normoblasts do not occur normally in new-born blood, and that their presence must be considered as a pathologic finding.

Schiff [3] experimented on the effect of tying the cord immediately after birth and found that the fall in the red blood count began during the first day. If, on the other hand, the cord was tied after the pulsation ceased, there was a rise in the red count lasting from three to four days, then the drop began and was continuous. In Schiff's work, the counts were all more than 6,000,000 on the first day. Even on the twelfth day after birth, the counts average 6,000,000 cells per cubic millimeter. The red blood counts taken during fasting were greater than after feeding. Viereck,[15] whose study was similar to that of Schiff, obtained quite different results. He found that when the cord was tied late, i. e., after pulsation had ceased, the red count began to descend early. He observed that in twelve cases there was a decrease, and in ten cases an increase in the count after feeding. If the blood was studied immediately after birth, the red blood cell count in the male new-born exceeded that of the female by 400,000.

Cathala and Daunay [16] found a physiologic increase in reticulated red cells at birth, up to 20 per cent. in a few cases. They obtained a decrease in the resistance of the red cells during the first few days after birth. This is in contrast to the observation of De Vicariis [17] who observed an increased resistance of the red blood corpuscles during the first few days.

Several theories have been advanced to explain the increased red blood cell count in the neonatal period. Schiff [3] claims it is due to a concentration of the blood brought about by increased excretion and decreased intake of fluids. Dupérié [18] accounts for the increased cell count by increased bone marrow activity. Hayem holds a similar view. Elder and Hutchison [19] agree with Schiff. They feel that the process must be due to concentration since it is too rapid for hemopoiesis or hemolysis. Hayem believes that the drop in the red blood cell count

---

12. Geissler and Japha: Beitrag zu den Anämien junger Kinder, Jahrb. f. Kinderh. **53**:627, 1901.

13. Hayem: quoted by Fehrsen.

14. Loos, J.: Ueber das Vorkommen kernhaltiger rother Blutzellen bei Kindern, Jahrb. f. Kinderh. **29**:331, 1895.

15. Viereck, H.: Beiträge zur Hämatologie des Neugeborenen, abstr. Folia. haematol. **1**:36, 1904.

16. Cathala, V., and Daunay, R.: Les hématies granuleuses, là resistance globulaire a la naissance et pendant les premièrs jours, Compt. rend. Soc. de Biol. **64**:801, 1908.

17. De Vicariis: Recherches sur le sang des enfants prematures, abstr. Zentralbl. f. norm. Anat. u. Mikrotchn. **3**:174, 1906.

18. Dupérié: quoted by Bayer.

19. Elder, G., and Hutchison, R.: Some Observations on the Maternal and Fetal Blood at Birth, Edinburgh M. J. **41**:105, 1895.

subsequent to the rise is due to the energetic building of other blood elements. Lépiné [20] accounts for the increased red count by a concentration. The drop is explained by a gain in weight and an increase in plasma. He found that while the weight of the new-born continues to drop the red count stays up. Gundobin [21] explains the change in the red count as being a result of a physiologic need, but the mechanism accounting for the changing counts is not described. Aitken [22] believes that the change in red count is due in part to a peripheral stasis of the blood and favors the concentration theory. Frank,[23] recently, in a paper on newborn blood also upholds the concentration view.

3. *The Blood Platelets.*—The literature on the blood platelets in the neonatal period is summarized in Table 1 and requires no special discussion at this point.

4. *The Leukocytes.*—A review of the literature is convincing that the new-born normally has an increased leukocyte count. Many causes have been advanced for this leukocytosis, the following being the more important ones.

(*a*) Blood Concentration: Just as in the case of the red blood cells, the small intake of food during a time in which the output of fluids goes on, causes a concentration of the blood and a rise in the leukocyte count. Schiff favors this view as being responsible, in part at least, for the increased white count.

(*b*) Inflow of Lymph Following Digestion: Schiff believes that in addition to blood concentration the lymph flow carries large numbers of lymphocytes into the circulation.

(*c*) Foreign Protein: As milk in an organism not fed before, Lépiné believes that this digestion has the power of causing the increased count.

(*d*) Peristence of Fetal Leukocytosis: Von Reuss [24] suggests that the condition of leukocytosis is present at birth and is carried over from the intra-uterine period. Scipiades [25] had previously presented this view.

---

20. Lépiné, R.: Blutkörperchen beim Neugeborenen, reviewed, Jahresb. ü. d. Leistung. in d. ges. Med. **1**:165, 1876.

21. Gundobin, N.: Ueber die Morphologie und Pathologie des Blutes bei Kindern, Jahrb. f. Kinderh. **35**:187, 1893.

22. Aitken, J.: Blood Counts in the New-Born, J. Obst. & Gynec. Brit. Emp. **1**:414, 1902.

23. Frank, M.: Beitrag zur Biologie der weiszen Blutzellen in der Neugeburtzheit und im Säuglingsalter, Ztschr. f. Kinderh. **31**:16 (Nov.) 1921.

24. Von Reuss, A. R.: The Diseases of the New-Born, New York, William Wood & Co., 1921, p. 41.

25. Scipiades, E.: Beiträge zur Physiologie des Blutes der Neugeborenen in den ersten zehn Lebenstagen, Arch. f. Gynaek. **70**:630, 1903.

(*e*) Traumatic Leukocytosis: Warfield [26] found in his cases that the leukocyte count was higher in difficult labors, so he suggests the possibility of a traumatic leukocytosis.

(*f*) Compensatory Leukocytosis: Arneth [27] believes the condition is due to a compensatory process to take the place of the liver and perhaps of the placenta which are active blood builders before birth. He thinks that the active hemopoiesis does not begin until the third or fourth day of life, when the bone marrow and other blood forming organs are able to take care of the blood formation.

(*g*) Leukocytosis Due to Circulatory Changes: Rieder [28] accounts for the leukocytosis by a sudden change of the circulation with its relations to the various organs.

(*h*) Bone Marrow Activity: Arneth.

(*i*) Pathologic Leukocytosis: According to Gundobin, the leukocytosis is a pathologic state due to a sudden deprivation of food derived through the placenta.

The effect of digestion on the leukocyte count has received much attention. Schiff found that the white count was usually highest after the first feeding. He also found a secondary rise present when the cord became detached. According to Wile,[29] digestive leukocytosis is uncommon in breast fed infants and inconstant in bottle fed infants and in early childhood. Karnitzki found the count to be greater before than after nursing. Warfield found during the first eight hours an average of 26,090 white cells. On the third day there was a decided drop to 13,270. On the eleventh day, due to the taking of more food than on the third day, the count was 16,740. Aitken cautions against the taking of white blood counts without regarding the relationship to food intake. His results are as follows: From two to sixteen hours—always before feeding—average, 18,525; second day, after feeding, 22,800; third day (relation to meals not noted) 15,585.

Aitken observed increases in his counts after feeding, averaging 10,000. Following a long fast, the digestive leukocytosis was found to be more marked. His increase in values varied from 5,000 to 17,000. Gundobin's findings in this regard are of interest. After fasting, he noted a polymorphonuclear leukocytosis. This was not observed until two or three hours after food was taken. The increase was less if there was a pre-existing leukocytosis. It averaged from 2,000 to 3,000. He

---

26. Warfield, L. N.: The Differential Leukocyte Count in the New-Born, Am. Med. **12**:457, 1902.

27. Arneth, J.: Die Leukocytose der Schwangerschaft, während und nach Geburt, und die Leukocytose der Neugeborenen, Arch. f. Gynaek. **74**:145, 1905.

28. Rieder: quoted by Carstanjen, Footnote 32.

29. Wile, I. S.: The Leukocytes in Pulmonary Diseases of Children. Arch. Pediat. **26**:195. 1909.

found that the time of day, temperature of the surroundings, weight of the child and muscular activity did not affect the leukocyte count. Japha [12] disagrees with Gundobin and failed to find a leukocytosis after food as a regular phenomenon. Mitchell [30] found that digestive leukocytosis was inconstant in babies. He observed increased leukocyte counts in the afternoon regardless of the taking of food. He often found a decreased value after feeding, though the count usually rose before the next feeding. When a rise was found after feeding, it occurred very soon after the food ingestion and began to decline in half an hour. Rieder, working on two cases, found an increase in mononuclear leukocytes after food was taken. Groeber [31] in ten cases decided that no conclusions could be made from his work. He found that in six cases, the polymorphonuclears were increased after food intake. In four cases they were decreased. Carstanjen [32] studied fifteen cases. Smears were studied before feeding, and one, two, three, four and five hours after feeding. The white counts are not given. The polymorphonuclears were always higher and the lymphocytes always lower before than after feeding. The average change was about 4 per cent., and was increased after a long fast. Aitken [22] found an increase in the polymorphonuclears of about 7 or 8 per cent. This was not marked on the second and third day.

5. *The Differential Leukocyte Count.*—With the rapid changing white blood count of the neonatal period there are equally marked changes in the differential blood picture, as seen in the outline. It is interesting to note the results obtained by Grüneberg [33] in his studies of the blood of the human embryo, which are instructive in showing the development of the blood picture present in the new-born. He found that at 3 months there are a large number of stem cells and only a few large lymphocytes. At this stage the blood closely resembles acute lymphatic leukemia. At from 5 to 6 months the stem cells become less numerous, and transitional leukocytes increase in number. At 7 months the stem cells reappear, and large numbers of polymorphonuclears are found, so that the picture resembles a mixed leukemia. Erythroblasts and megaloblasts are very commonly seen during the first 3 months, but after this period megaloblasts are rarely seen. Atypical cells pass into the circulation during the ninth fetal month.

---

30. Mitchell, A. G.: Leukocyte Counts During Digestion in Bottle-Fed Infants, Am. J. Dis. Child. **9**:358 (May) 1915.

31. Groeber: quoted by Carstanjen, Footnote 32.

32. Carstanjen, M.: Wie verhalten sich die prozentigen Verhältnisse der verschiedenen Formen der weissen Blütkörperchen beim Menschen unter normalen Verhältnissen, Jahrb. f. Kinderh. **52**:215-333 1900.

33. Grüneberg, A.: Beitrag zur Morphologie des Blutes menschlichen Embryonen, abstr. Folia Haematol. **6**:185, 1908-1909.

MATERIAL AND METHODS

1. *Time Intervals Employed.*—Seventy-one new-born infants (thirty-one girls and forty boys) were used for the present study.

Examinations were made as soon after birth as possible, and then at approximate six hour intervals up to and including thirty-six hours. The next examination was at forty-eight hours, and a final examination was made at 5 days of age to determine the direction of the curves for the white count, and the various components of the differential.

It was very difficult to study the blood at the exact hourly intervals, so for convenience the following range of hours was used: (1) At birth to one and one half hours after birth, median, one half hour; (2) from five to seven hours after birth, median, six hours; (3) from eleven to thirteen hours after birth, median, twelve hours; (4) from fifteen to twenty-one hours after birth, median, eighteen hours; (5) from twenty-three to twenty-five hours after birth, median, twenty-four hours; (6) from twenty-nine to thirty-one hours after birth, median, thirty hours; (7) from thirty-four to thirty-eight hours after birth, median, thirty-six hours; (8) from forty-six to fifty hours after birth, median, forty-eight hours; (9) five days after birth.

In every case the cord was clamped after pulsation had ceased, the average time being about from two to four minutes.

More than 50 per cent. of the mothers were gravida. In those who had a history of miscarriages, the venereal history of the father, mother and others in the family was thoroughly investigated. Syphilis was absent in all of the cases studied. The mother's urine was examined and in every case was negative except for occasional lactosuria, a trace of albumin or a few leukocytes.

2. *Selection of Material.*—The question of choosing a new-born fitted for study was often difficult. The skin offered an occasional problem. Impetigo of a mild degree was encountered in several cases. Desquamation or generalized dermatitis, lasting for short periods and then disappearing, was not thought sufficient cause for rejection of new-borns.

Temperature elevation cannot be used as a guide for inflammatory conditions because of its frequency in apparently normal new-born children. In many cases, the giving of a few ounces of water caused a drop in the temperature; to be explained on the basis of dehydration. As regards the eye discharges, those cases were included which failed to show bacteria on repeated examinations.

Eclampsia in the mother was in itself not considered sufficient cause for rejection, so long as the infant was entirely normal.

In two instances, tuberculosis was present in the mother. In one case an arrested tuberculous pulmonary infection was present, while the

other patient died shortly after childbirth, the cause of death being tuberculous meningitis. The two babies were normal in every respect, the tuberculin reactions were normal, and the gain in weight satisfactory so they were included in the study.

The cases excluded as abnormal were: Those in whom definite infection was proved, any new-born that weighed less than 2,500 gm. was considered premature and not included in the group, and new-born babes with hemorrhagic disease.

Icterus neonatorum was not found to be a cause for excluding the new-born. Almost every baby has some degree of icterus during the first few days. In a few babies with severe icterus the findings were tabulated to compare them with the findings in those who did not show marked icterus.

3. *Hemotologic Technic.*—The blood was obtained in the usual way by pricking the heel. The part was first cleansed with alcohol and ether, and a free flow of blood was always obtained. The first two drops were not used. The blood for study was secured when it flowed without the aid of external pressure.

For the study of the red blood cells Deiner's solution was used. The blood was drawn to 0.5 in the 1 : 100 dilution pipette, and the Deiner's solution was then drawn to 100, making a dilution of 1 : 200. The pipette was shaken for at least five minutes to keep the platelets from clumping. Thus the red cells and platelets were obtained in the one pipette. At first the white cell pipette for 1 : 10 dilution and the red cell pipette for 1 : 100 dilution were both used for the white cell count; with the two different dilutions the counts could be checked. Later, however, this was not done and the 1 : 100 dilution alone was used, for the latter method was found after repeated trials to be the more accurate. The Levy-Zeiss hemocytometer was employed, and in every case repeated drops from the same pipette were used to check results. The pipettes used were standardized, and checked against each other.

Smears of various degrees of thickness were made for differential cell counts and finer cytology. The smears were stained with Wright's modification of the Romanowsky dye. Five hundred cells were included in each differential count.

The complete individual differential counts have been placed on file at the Wistar Institute of Anatomy, Philadelphia.

4. *Classification of Leukocytes and Erythroblasts.*—Throughout the discussion Pappenheim's [34] terminology has been used, the following criteria being used for determining the different types of cells.

34. Pappenheim, A.: Clinical Examination of the Blood and Its Technique, New York, William Wood Co., 1914.

(*a*) The Neutrophil, i. e., Polymorphonuclear P. M. N. Leukocyte: The nucleus is lobulated. The cytoplasm is acidophilic, stains pink with Wright's stain, and contains all types of pink granules. Some of these cells contain vacuoles in their cytoplasm.

(*b*) The Lymphocytes: The lymphocytes have been divided into four classes: (1) The small lymphocyte. The nucleus is coarse, and occupies most of the cell. It is surrounded by a narrow rim of greenish blue cytoplasm which may, but usually does not, contain azure granules; (2) the medium lymphocyte. This cell is classified according to size rather than structure. It is about twice the size of a normal red blood cell. The nucleus may form only one half of the cell but often it very nearly fills the cell, much as in the case of the small lymphocyte. The cytoplasm and nuclear structures are as in the small lymphocyte; (3) the large lymphocyte. This term is used to denote the macrolymphocyte of Pappenheim. The nucleus is small, in a cell about the size of the polymorphonuclear. The structure of the nucleus is like that of the small lymphocyte (Fig. 1 *a*); (4) the leukocytoid mesolyphocyte. Much the same as 3 except that the nucleus is smaller and less dense (Fig. 1 *b*).

In addition to the above, one often sees younger lymphocytes. These are recognized by the open structure of the nucleus. The chromatin strands are arranged as in a sieve. Usually nucleoli are present in the nucleus (Fig. 1 *c*). One can easily differentiate this nucleus from that of an adult lymphocyte (Fig. 1 *a*) in which the chromatin is arranged in coarse clumps. In the case of the Türke cell, the nucleus is of the early type, and is situated eccentrically.

Lymphocytes having undergone division often appear in the blood stream. The cell is usually large and contains two similar nuclei (Fig. 1 *d*).

(*c*) The Large Mononuclear Leukocyte: The cell is about the size of a large lymphocyte. The cytoplasm is usually a pale blue-green. The nucleus occupies a great part of the cell and has a moderately open chromatin network as compared with Figures 1 *a* and 1 *c*.

(*d*) The Transitional Leukocyte: The cell contains a horseshoe shaped nucleus in a green-blue cytoplasm. It is about the size of a large mononuclear leukocyte. The granules present in cells with basophilic cytoplasm described above are azure. They may be fine, medium, or coarse and are present in varied arrangements. Usually they are more numerous in the larger cells of this group.

(*e*) The Eosinophilic Polymorphonuclear Leukocyte: The nucleus is similar to that of the P. M. N. neutrophil. The cytoplasm is usually filled with coarse red granules.

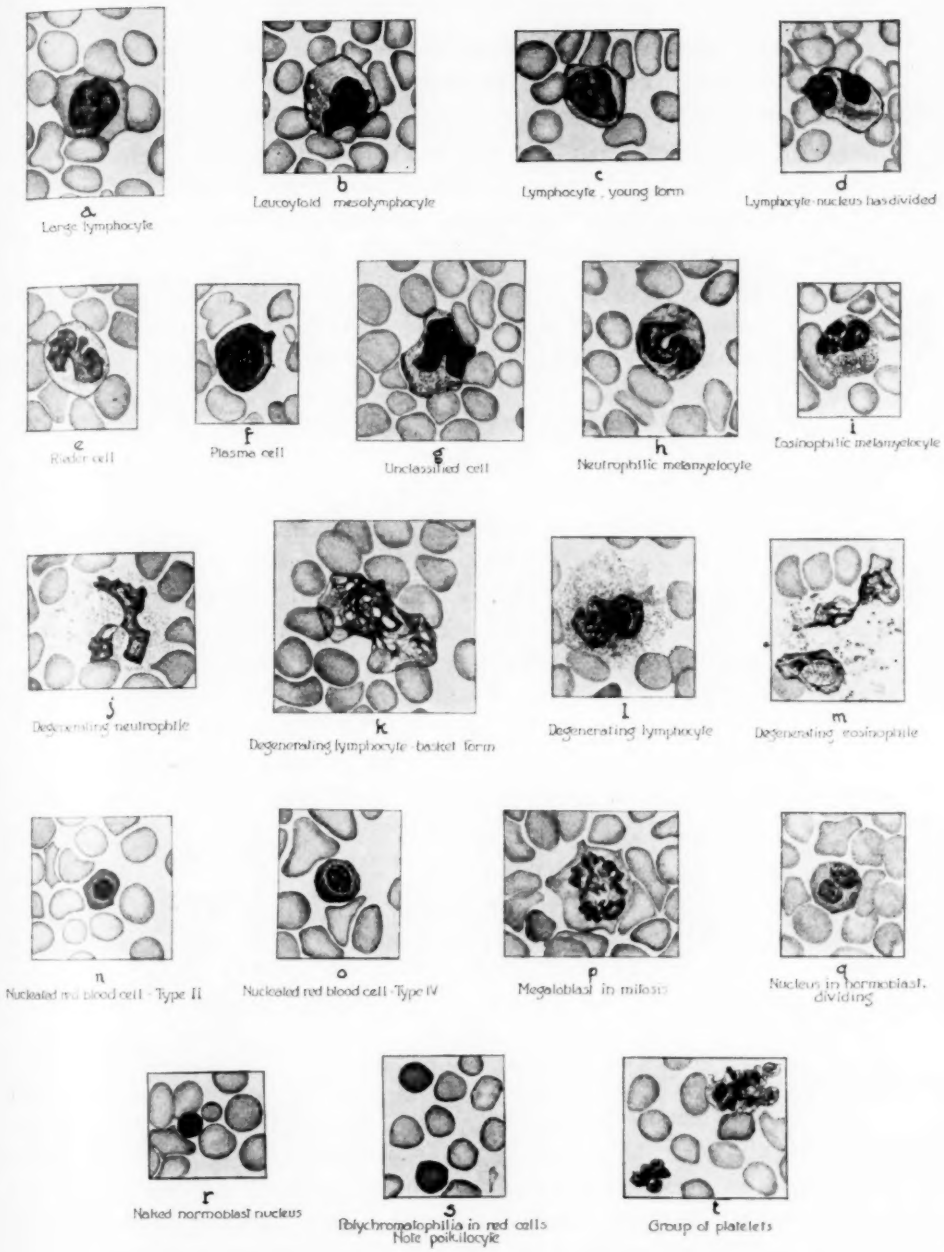

Fig. 1.—(*a*) Large lymphocyte, (*b*) leukocytoid mesolymphocyte, (*c*) lymphocyte—young form, (*d*) lymphocyte—nucleus has divided, (*e*) Rieder cell, (*f*) plasma cell, (*g*) unclassified cell, (*h*) neutrophilic metamyelocyte, (*i*) eosinophilic metamyelocyte, (*j*) degenerating neutrophil, (*k*) degenerating lymphocyte—basket form, (*l*) degenerating lymphocyte, (*m*) degenerating eosinophil, (*n*) nucleated red blood cell, Type II, (*o*) nucleated red blood cell, Type IV, (*p*) megaloblast in mitosis, (*q*) nucleus in normoblast dividing, (*r*) naked normoblast nucleus, (*s*) polychromatophilia in red cells (note poikilocyte), (*t*) group of platelets.

(*f*) The Basophilic Polymorphonuclear Leukocyte: The nucleus is usually irregular and pale. The granules stain a purplish blue.

(*g*) The Rieder Cell: The cytoplasm is basophilic. The nucleus is irregular, usually indented on both sides. It is distinctly an irritation type of cell (Fig. 1 *e*). The same nucleus may be present in a cell with neutrophilic cytoplasm, in which case the cell is a Rieder cell in the myeloid series.

(*h*) The Plasma Cell: The cytoplasm is a very deep blue and contains no granules. The nucleus has a cart wheel structure and is usually eccentrically placed (Fig. 1 *f*).

(*j*) The Unclassified Cell: So called because it could not be included in the classification of Pappenheim. It is apparently an irritation type. The cell is about the size of a large mononuclear leukocyte. The nucleus is usually single but it is twisted on itself in an irregular manner, or may be broken up into two unequal parts. The cytoplasm is a muddy, bluish red, and contains both coarse and medium azure granules as well as dust-like neutrophilic granules, like those seen in the neutrophilic promyelocyte. Probably the cell represents a promyelocyte stage in which the nucleus is developing at a greater rate than the cytoplasm (Fig. 1 *g*).

(*j*) The Neutrophilic Myelocyte: Its size is that of a P. M. N. neutrophil. The structure of the two cells is similar except that the nucleus in the myelocyte is not lobed and is less dense.

(*k*) The Eosinophilic Myelocyte: The same as eosiniphilic P. M. N. except that the nucleus is not lobed.

(*l*) The Neutrophilic Metamyelocyte: This includes all neutrophilic cells in which the nucleus is not spherical, but is still undivided. All shapes of nuclei are observed; the one most commonly seen is shown in Figure 1 *h*. Many of these cells are in reality irritation types of P. M. N. neutrophils, but are classed as metamyelocytes because the nucleus is not lobed.

(*m*) The Eosinophilic Metamyelocyte: An eosinophil with a horseshoe shaped nucleus (Fig. 1 *i*).

(*n*) Degeneration Forms: (1) The neutrophilic leukocytes are of several types. The most common one has a dark, fairly easily recognizable nucleus surrounded by groups of neutrophil granules in an irregular mass of cytoplasm. Often a large fan-like mass of light staining substance projects from the end of one of the nuclear fragments (Fig. 1 *j*); (2) the lymphocytes, the form most commonly met, is the large basket-like form with no definite structure present. At times, one sees the beginning formation of the basket effect from one corner of the

nucleus of an otherwise fairly intact lymphocyte. One occasionally sees a fairly normal lymphocyte nucleus surrounded by small masses of greenish cytoplasm. Still another type is the ragged, irregular lymphocyte nucleus without any surrounding cytoplasm (Fig. 1 *k* and l); (3) in the eosinophilic leukocytes, one sees a fairly intact nucleus surrounded by irregularly scattered, large, eosinophil granules. The granules often stain darker than normal eosinophil granules. Here too, the nucleus may be breaking up into a basket form (Fig. 1 *m*).

(*o*) The Nucleated Red Blood Cells: For convenience these are divided into four groups: (1) The cytoplasm is red, i. e., contains hemoglobin. The nucleus is condensed. (2) The cytoplasm is polychromatophilic. The nucleus is condensed (Fig. 1 *n*). (3) The cytoplasm is red. The nucleus has an open structure. (4) The cytoplasm is polychromatophilic. The nucleus is similar to that in 3 (Fig. 1 *o*). The term megaloblasts is used for enlarged, nucleated red blood cells. These may be classed 1, 2, 3 or 4.

In addition, one sees an occasional mitotic figure in the nucleated red blood cells (Fig. 1 *p*).

5. *Numerical and Graphical Treatment of Data.*—Since a considerable portion of this work deals with the numerical consideration of the absolute and relative number of the various types of cells in the blood stream, it is important that these figures are examined with some of the simpler analytic and graphic methods which are now applied to biologic problems of this nature. The following program of analysis was therefore carried out in connection with this material.

(*a*) The observations for each of the various types of cells studied were grouped in their time intervals, as outlined in the preceding section, and the central tendency and the dispersion of the data determined. The central tendency was calculated by two methods; first, by the usual arithmetic mean or average; and second, by the median. The determination of the average needs no description but the median is less familiar. The median is the middle value in a series of observations. It is determined by arranging the observations in order of magnitude from the smallest to the largest, and establishing the middle observation by counting from either end of the series. In a large series of observations, if the distribution of cases is symmetrical, the median will approach closely the average. In most series of observations, the number of cases and the character of the distribution does not produce a median exactly equivalent to the average, but the measure is often of value because it does not overemphasize the extreme cases in the group. The dispersion of the data from the average was determined by computing the standard deviation and the coefficient of variability. The standard deviation,

which is now recognized as a routine method of determining the absolute variability of a value, is the square root of the average of the squares of the departure of each observation from the average of the entire series of observations. It is commonly expressed by the formula:

$$SD = \sqrt{\frac{d^2}{N}}$$

where SD is the standard deviation, d^2 is the sum of the squares of the deviations of the individual observations from the average and N is the number of the cases in the series. The standard deviation is an absolute number, such as grams if the original observations are in grams, or centimeters if they are in centimeters. To reduce this to a relative number, in the form of a percentage of the average, so that the variabilities of unlike values may be compared, the standard deviation is converted into the coefficient of variability by the formula:

$$CV = \frac{SD}{A} \times 100$$

where CV is the coefficient of variability, SD is the standard deviation and A is the average of the series of observations. In other words, the coefficient of variability is the standard deviation divided by the arithmetic mean or average and multiplied by 100 to put the result in the form of a per cent. of the average.

(*b*) The data and results of this series of computations were placed in graphic form by plotting two series of charts. The first series are field charts having one sort of abcissae (time in hours) and two sets of ordinates (absolute and percentage number of cells). The individual counts were plotted on the fields thus established; the solid dots being used to indicate the relative cell count, and the open circles the absolute cell count.

In the second series of charts the abcissae and ordinates were drawn as in the preceding, and the absolute averages and the percentage averages were indicated by point to point curves, solid lines being used for the former and broken lines for the latter.

(*c*) The results expressed graphically in the series of charts were arranged in tabular form and constitute Tables 2 to 18 of the present study. These tables include the following data: (1) the range and the median of the time intervals used in the study, (2) the number of cases for each interval, (3) the central tendency of both the absolute and percentage values for each interval, (4) the variability as indicated by the maximum and minimum values in each given set of observations as, and (5) the degree of variability as indicated by the standard deviation and the coefficient of variability.

OBSERVATIONS

1. *The Red Blood Cell Count.*—The values of the red blood cell counts obtained are shown in Figures 2 and 3 and in Table 2. The curve of the red count at the different time intervals (Fig. 3), shows

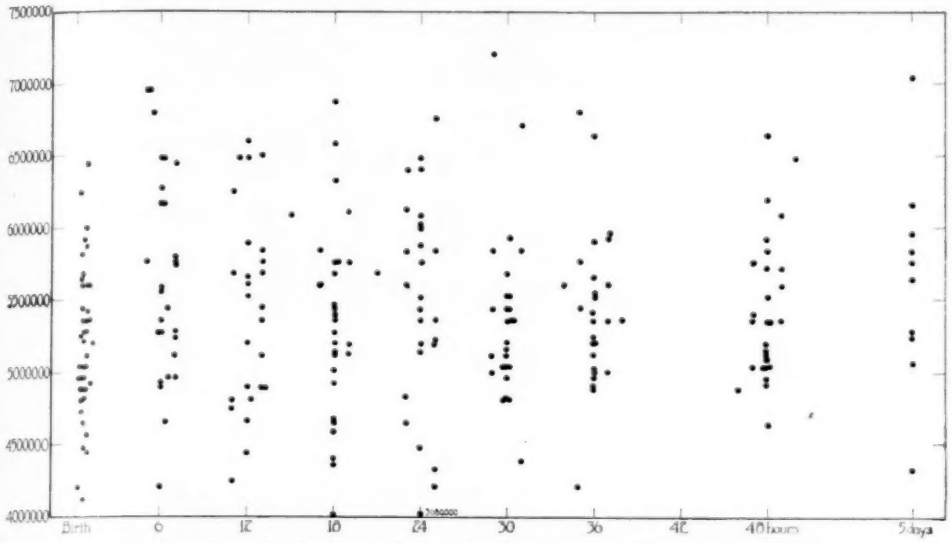

Fig. 2.—The distribution of the absolute counts of red blood cells.

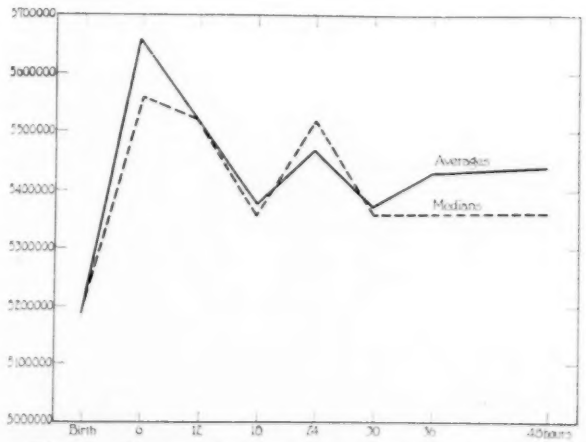

Fig. 3.—The absolute counts of red blood cells.

a marked rise during the first six hours, from 5.2 to 5.65 million. This is temporary, for, at twelve hours a definite drop has occurred. This decline continues until eighteen hours after birth, after which time the count remains about the same as that of the eighteen hour period, 5.4

million. The early ascent is interesting and corresponds to the rise obtained by other investigators. It is unlike the rise taken by the leukocytes which continues until twelve hours after birth. These counts are not nearly so high as those of many other observers, and in most cases the maximum figures correspond fairly closely with other observer's averages. The median curve follows the average curve.

TABLE 2.—*Red Blood Corpuscles Per Cubic Millimeter*

Age (Hours)								
Median	Range	Average (Million)	Median (Million)	Maximum (Million)	Minimum (Million)	Standard Deviation (Thousands)	Coefficient of Variability	Number of Cases
0.5	0 to 1.5	5.19	5.22	6.44	4.12	51.62	9.93	41
6	5 to 7	5.66	5.56	6.96	4.20	70.39	12.44	28
12	11 to 13	5.52	5.52	7.60	4.24	68.95	12.49	27
18	15 to 21	5.38	5.36	6.88	4.00	65.06	12.09	30
24	23 to 25	5.47	5.52	6.76	3.68	74.25	13.57	27
30	29 to 31	5.37	5.36	7.20	4.38	57.23	10.66	27
36	34 to 38	5.43	5.36	6.80	4.20	52.07	9.59	27
48	46 to 50	5.44	5.36	6.64	4.64	49.15	9.03	28

2. *The Platelet Count.*—Variations of from 10 to 20,000 platelets per cubic millimeter can be considered within the limits of mechanical error because of the difficulty in making this type of count. At birth, as can be seen in Figures 4 and 5 and Table 3, the count is highest, the average being 213,000. During the first six hours there is a sudden drop in the number of platelets, followed by a slower decrease until eighteen hours after birth, and then by a tendency to increase slowly.

TABLE 3.—*Platelets Per Cubic Millimeter*

Age (Hours)								
Median	Range	Aver-age	Median	Maxi-mum	Mini-mum	Standard Deviation (Thousands)	Coefficient of Variability	Number of Cases
0.5	0 to 1.5	213,000	196,000	500,000	112,000	91.1	42.8	41
6	5 to 7	179,000	160,000	346,000	108,000	65.2	36.4	28
12	11 to 13	181,000	156,000	460,000	101,000	83.4	46.1	27
18	15 to 21	172,000	165,000	324,000	100,000	52.5	30.3	30
24	23 to 25	191,000	164,000	372,000	103,000	77.1	40.4	27
30	29 to 31	186,000	176,000	330,000	90,000	59.4	31.9	27
36	34 to 38	180,000	165,000	290,000	82,000	51.3	28.5	27
48	46 to 50	192,000	180,000	348,000	95,000	55.2	28.8	28

In the few cases of icterus neonatorum of marked degree, neither the decrease in platelet count observed by Heimann [35] nor the increase described by Morse [36] was found. The averages tend to be the same as in the normal. Nothing unusual in this regard was noted the first two days before the icterus became marked.

35. Heimann, F.: Zur Lehre des Icterus Neonatorum, Ztschr. f. Geburtsh. u. Gynäk. **69**:165, 1911.

36. Morse, M.: The Blood Platelets in Normal Women, in Obstetrical Patients, and in the New-Born, Boston M. & Surg. J. **166**:448, 1912.

3. *The Total Leukocyte Count.*—By far the most interesting phase in the study of new-born blood is that of the white cell count and differential. Figures 6 and 7 and Table 4 show the leukocyte counts at the different time intervals.

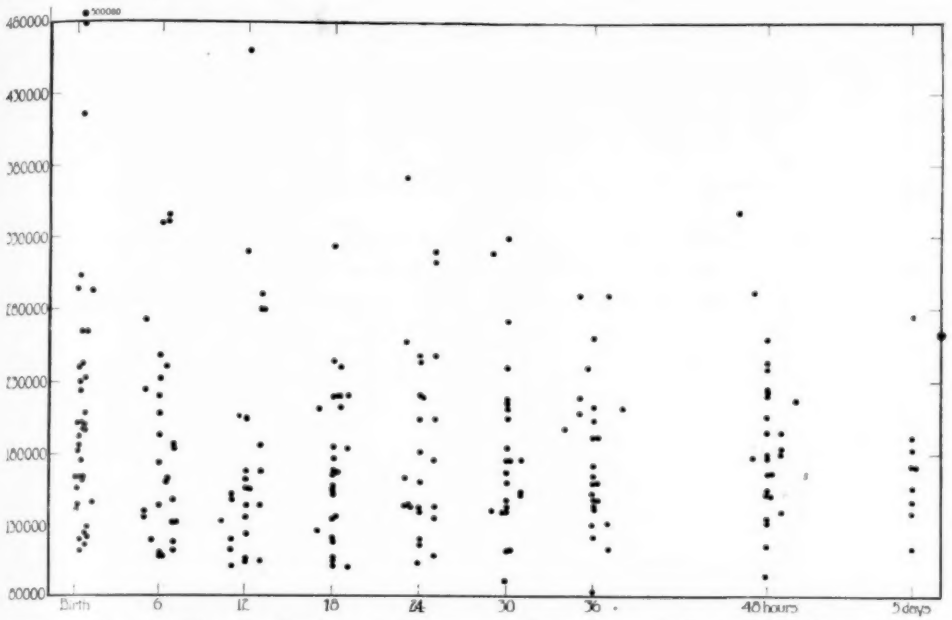

Fig. 4.—The distribution of the counts of absolute number of platelets.

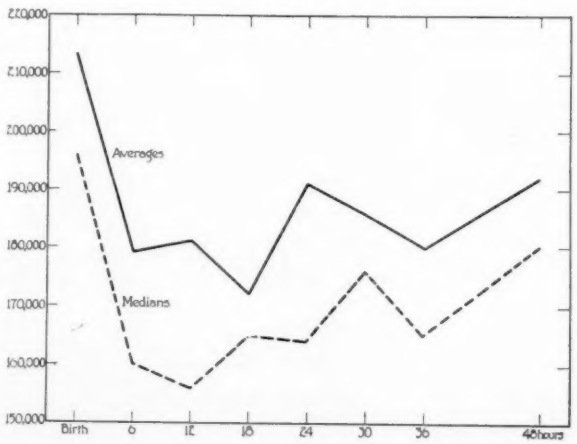

Fig. 5.—The absolute counts of platelets.

At birth, the count is almost always higher than in the normal adult, the average being 16,000. The count rises rapidly until six hours after

birth, it then rises at a slower rate, until twelve hours after birth, when it is 22,500. After this period there is a definite descent at about the same rate as that of the ascent. Between twenty-four and thirty hours

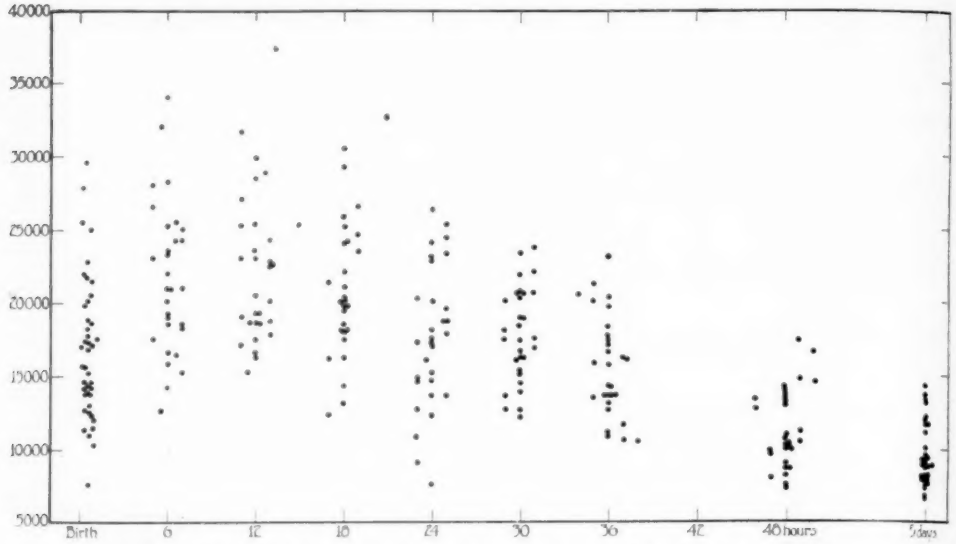

Fig. 6.—The distribution of absolute counts of white blood corpuscles.

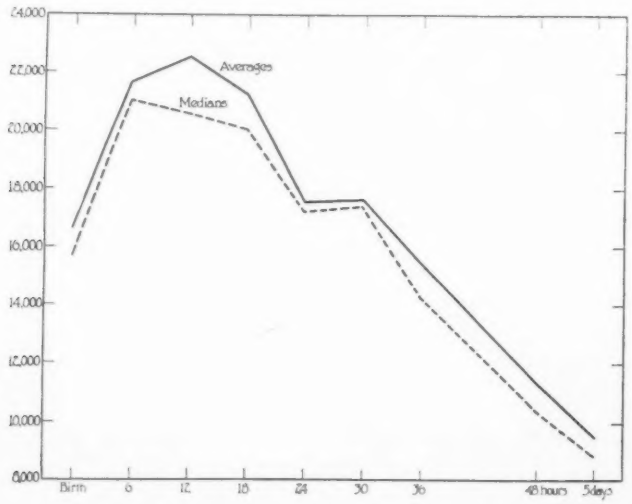

Fig. 7.—The absolute counts of white blood corpuscles.

the count is almost stationary but thereafter there is a gradual fall until five days after birth.

TABLE 4.—*White Blood Corpuscles Per Cubic Millimeter*

Age (Hours)		Average	Median	Maximum	Minimum	Standard Deviation (Thousands)	Coefficient of Variability	Number of Cases
Median	Range							
0.5	0 to 1.5	16,600	15,700	29,600	7,600	5.18	31.2	42
6	5 to 7	21,000	21,000	34,000	12,600	5.08	23.5	30
12	11 to 13	22,500	20,500	37,500	15,200	5.26	23.4	30
18	15 to 21	21,200	20,000	30,400	12,200	4.52	21.3	30
24	23 to 25	17,500	17,200	26,200	7,500	4.70	26.9	30
30	29 to 31	17,600	17,400	23,600	12,000	4.20	23.9	30
36	34 to 38	15,400	14,200	23,000	10,400	3.46	22.5	30
48	46 to 50	11,300	10,300	17,200	7,200	2.61	23.1	30
5 days		9,500	8,800	14,200	6,500	2.52	26.5	30

4. *The Differential Leukocyte Count.*—The average differential leukocyte count follows a definite course during the first few days of postnatal life, but the individual counts show a high degree of variability.

Occasionally there is little difference in the differential study from one period to another in the first eighteen hours, usually there is a rapid change in the blood picture.

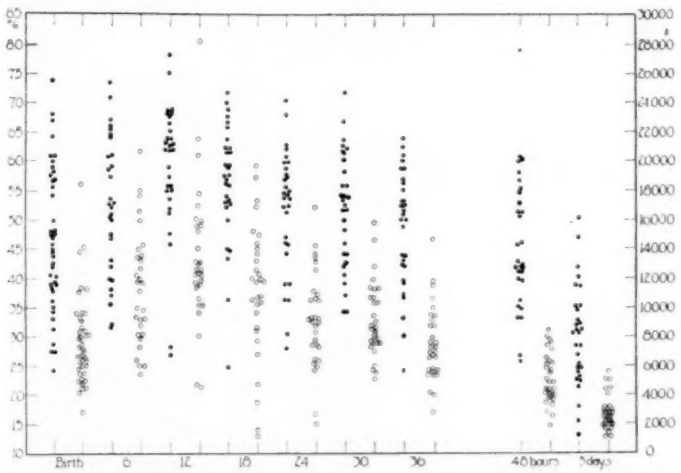

Fig. 8.—The distribution of absolute and percentage counts of polymorphonuclear neutrophil leukocytes. Solid dots, percentage counts; circles, absolute counts.

(*a*) The Polymorphonuclear Neutrophilic (P. M. N.) Leukocytes: A study of the P. M. N. neutrophils is very interesting, since these cells apparently determine the fluctuating white cell count. Figures 8 and 9 and Table 5 indicate that when the percentage values of the P. M. N.'s are averaged, a curve is obtained which shows an ascent until twelve hours after birth, followed by a slow descent. However, when the absolute values are studied, one finds a curve almost identical with that of the total white count.

(*b*) The Neutrophilic Metamyelocytes: As has been previously mentioned, these cells differ from the P. M. N. neutrophil in that their nucleus is single but not spherical. Figures 10 and 11 and Tables 6 show that the incidence of these cells follows very closely that of the P. M. N. neutrophils, with the exception that the apex of the curve occurs at six hours and a slight secondary rise occurs at eighteen hours after birth. After this, there is a gradual descent of the curve.

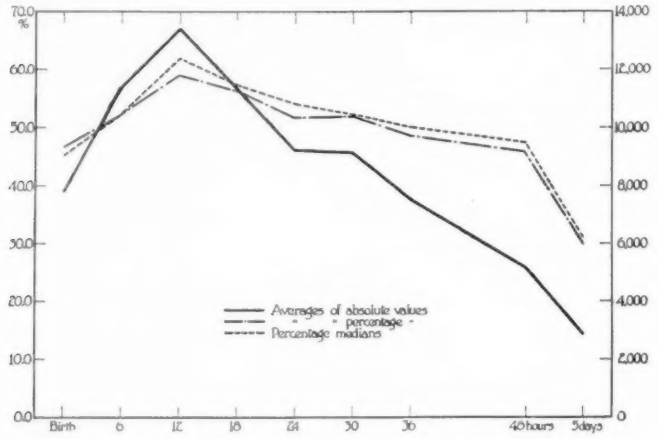

Fig. 9.—Absolute and percentage counts of polymorphonuclear neutrophil leukocytes.

TABLE 5.—*Absolute and Percentage Number of Polymorphonuclear Neutrophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	46.7 **7,788**	45.4 **7,257**	74.0 **18,500**	27.2 **2,823**	12.040 **2,975**	25.8 **38.15**	40
6	5 to 7	52.3 **11,425**	52.2 **11,900**	73.4 **20,740**	32.0 **5,411**	11.557 **3,850**	22.1 **33.70**	30
12	11 to 13	59.1 **13,491**	62.0 **12,728**	78.2 **28,200**	26.8 **4,422**	11.229 **4,890**	19.0 **36.25**	30
18	15 to 21	56.4 **11,264**	57.4 **11,886**	71.8 **19,797**	24.6 **1,272**	9.569 **4,508**	17.0 **40.02**	30
24	23 to 25	51.6 **9,207**	54.0 **9,106**	70.4 **16,896**	28.6 **2,145**	10.311 **3,255**	20.0 **35.35**	30
30	29 to 31	51.9 **9,177**	52.4 **8,694**	71.6 **15,812**	34.4 **5,136**	9.630 **2,547**	18.6 **27.75**	30
36	34 to 38	48.6 **7,540**	50.0 **7,504**	63.8 **14,674**	24.4 **2,806**	9.982 **2,548**	20.5 **33.79**	30
48	46 to 50	45.9 **5,161**	42.4 **4,809**	74.0 **8,429**	25.8 **1,929**	3.319 **1,714**	7.2 **33.21**	30
5 days		30.0 **2,895**	30.8 **2,898**	50.4 **5,491**	13.0 **1,185**	8.413 **1,171**	28.0 **40.44**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

Here, as in other curves, one can see the value of obtaining the absolute cell counts, which are considerably different from those of the percentage values.

In one case (45), 8.5 per cent. of the leukocytes were metamyelocytes at birth, whereas at eighteen hours, with approximately the same

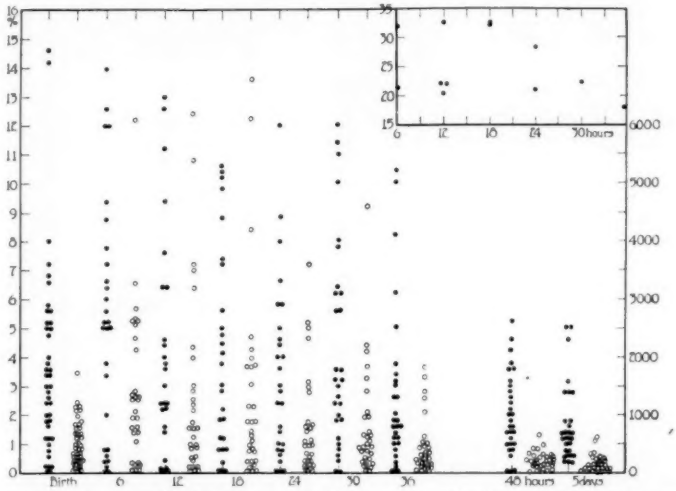

Fig. 10.—The distribution of absolute and relative counts of neutrophil metamyelocytes. Solid dot, percentage counts; circles, absolute counts.

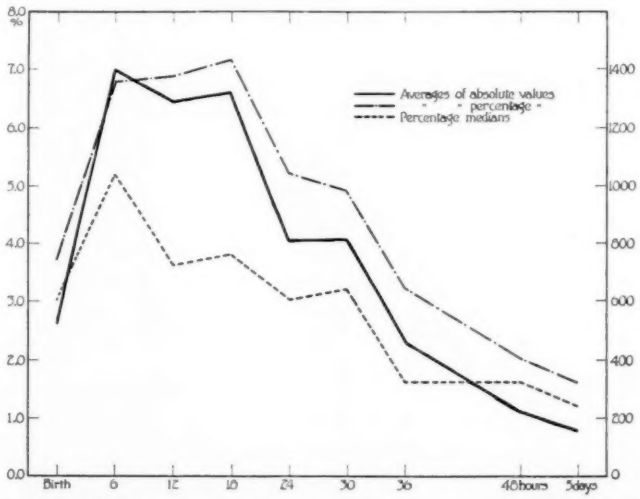

Fig. 11.—Absolute and percentage counts of neutrophil metamyelocytes.

total number of leukocytes, there was 43.0 per cent. metamyelocytes, the highest percentage of this cell observed in the present study.

(*c*) The Neutrophilic Myelocytes: These are not so commonly met as one would expect from the large numbers of metamyelocytes. During the first twelve and eighteen hours they are occasionally seen, but

TABLE 6.—*Absolute and Percentage Number of Neutrophil Metamyelocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.7 **520**	3.0 **432**	14.6 **1,732**	0.0 **0.0**	3.178 **620.26**	85.89 **119.28**	42
6	5 to 7	6.8 **1,399**	5.2 **1,260**	32.0 **6,080**	0.0 **0.0**	6.735 **1294.81**	99.04 **92.55**	30
12	11 to 13	6.9 **1,293**	3.6 **756**	32.6 **6,160**	0.0 **0.0**	7.53 **1553.92**	108.74 **117.10**	30
18	15 to 21	7.2 **1,327**	3.8 **876**	43.0 **6,804**	0.0 **0.0**	10.344 **1647.78**	143.66 **124.17**	30
24	23 to 25	5.2 **804**	3.0 **496**	28.2 **3,570**	0.0 **0.0**	6.398 **851.76**	123.03 **106.47**	30
30	29 to 31	4.9 **814**	3.2 **450**	22.4 **4,592**	0.0 **0.0**	4.751 **925.25**	96.96 **113.67**	30
36	34 to 38	3.2 **459**	1.6 **314**	18.0 **2,340**	0.0 **0.0**	3.870 **540.38**	120.93 **117.73**	30
48	46 to 50	2.0 **213**	1.6 **202**	5.2 **650**	0.0 **0.0**	1.319 **131.26**	65.95 **61.62**	30
5 days		1.6 **155**	1.2 **95**	5.0 **607**	0.0 **0.0**	1.322 **139.14**	82.62 **89.77**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

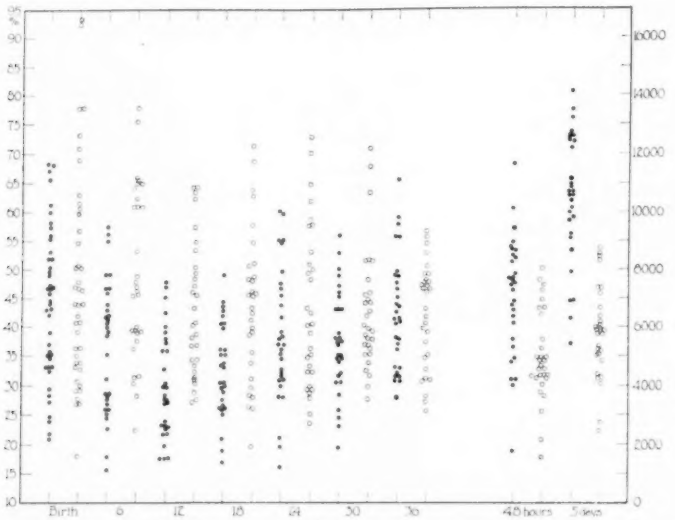

Fig. 12.—The distribution of absolute and percentage counts of combined lymphocytes. Solid dots, percentage counts; circles, absolute counts.

after this time they are rare. A curve of their incidence was not made, because of their infrequent occurrence.

(*d*) The Lymphocytes: The percentage of lymphocytes is fairly high (44.7 per cent.) at birth. The values first descend until twelve hours after birth, and then ascend gradually. They are at the peak of the curve after five days. Figures 12 and 13 and Table 7 show how easily one may be misled by relying on percentage values. When this curve is compared with the curve of P. M. N. percentages one sees that the two are almost the reverse of each other. At forty-eight hours they equal each other, after which time the percentage of lymphocytes is greater than that of the neutrophils (Fig. 14).

On the other hand, on plotting the absolute values of the lymphocytes, one sees an entirely different result. The highest values are present during the first six hours, and after this there is a gradual decrease in the absolute number until forty-eight hours. A slight secondary rise occurs between forty-eight hours and five days.

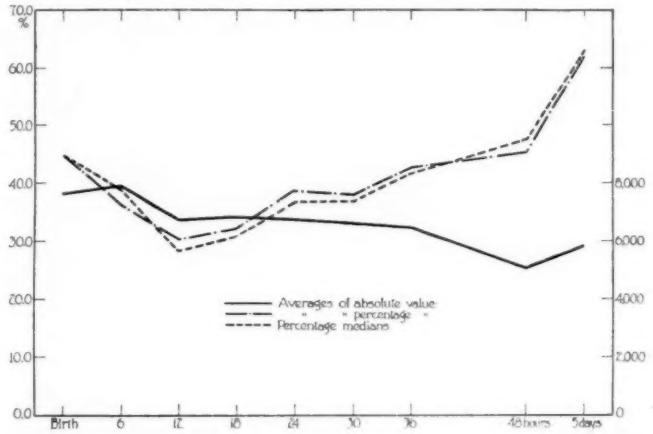

Fig. 13.—Absolute and percentage counts of combined lymphocytes.

TABLE 7.—*Absolute and Percentage Number of Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	44.7 **7,618**	44.6 **6,832**	67.2 **16,680**	21.2 **1,647**	13.481 **3,545**	30.16 **46.54**	42
6	5 to 7	36.4 **7,690**	38.8 **7,445**	57.0 **13,648**	15.6 **2,556**	11.157 **2,907**	30.65 **36.85**	30
12	11 to 13	30.1 **6,704**	28.4 **6,256**	47.2 **10,986**	17.6 **3,560**	10.381 **2,286**	34.49 **34.10**	30
18	15 to 21	32.1 **6,848**	30.8 **7,120**	49.4 **12,342**	9.8 **2,058**	8.761 **2,558**	27.29 **37.36**	30
24	23 to 25	38.7 **6,766**	37.0 **6,271**	60.2 **12,650**	16.4 **2,898**	10.939 **2,741**	28.27 **40.51**	30
30	29 to 31	38.0 **6,672**	37.0 **6,160**	56.2 **12,251**	19.6 **3,600**	8.788 **2,054**	23.13 **30.78**	30
36	34 to 38	42.9 **6,540**	41.8 **7,314**	65.6 **9,402**	28.2 **3,297**	9.119 **1,759**	21.26 **26.89**	30
48	46 to 50	45.8 **5,110**	48.0 **4,989**	68.0 **8,187**	19.2 **1,632**	10.240 **1,527**	22.36 **29.89**	30
5 days		62.4 **5,924**	63.2 **5,985**	80.8 **8,860**	37.4 **2,505**	11.118 **1,540**	17.82 **26.00**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

When the various types of lymphocytes are graphed one obtains curves which are very similar. In the case of the small lymphocytes (Figs. 15 and 16 and Table 8) there is a secondary rise at twenty-four hours followed by a gradual fall. The small lymphocytes are, as a rule, fully twice as numerous as the large lymphocytes. The leukocytoid mesolymphocytes are not so commonly seen as are the large lymphocytes.

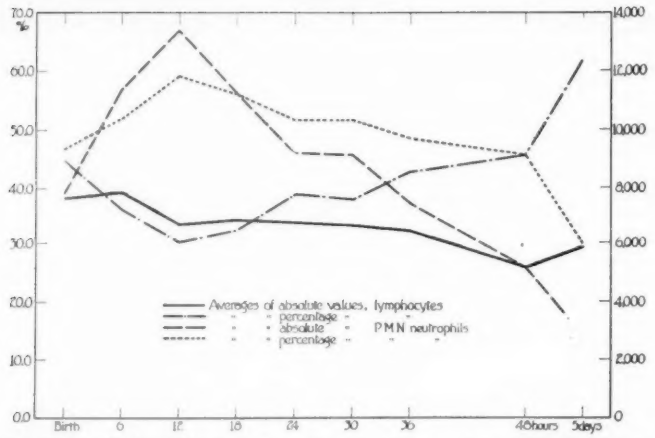

Fig. 14.—The relationship between the absolute and percentage counts of the polymorphonuclear neutrophil leukocytes and the lymphocytes. Solid line, average of absolute counts of lymphocytes; dot and dash line, average of percentage counts of lymphocytes; broken line, average of absolute counts of polymorphonuclears; dotted line, average of percentage counts of polymorphonuclears.

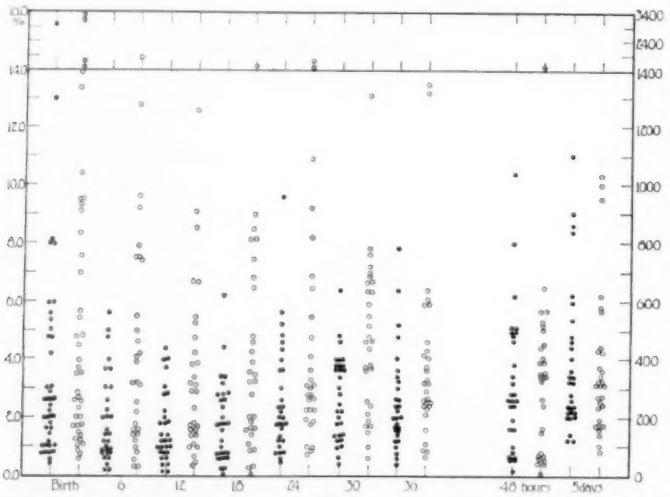

Fig. 15.—The distribution of absolute and percentage counts of small lymphocytes. Solid dots, percentage counts; circles, absolute counts.

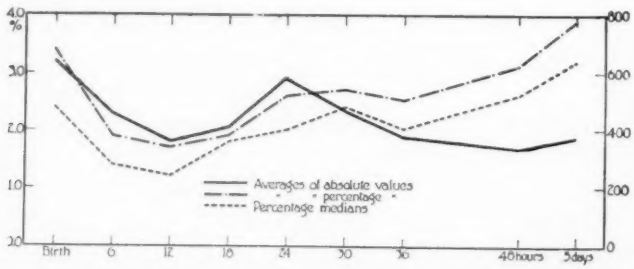

Fig. 16.—Absolute and percentage counts of small lymphocytes.

TABLE 8.—*Absolute and Percentage Number of Small Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.4 **636**	2.4 **268**	15.6 **3,315**	0.4 **61**	3.228 **714.61**	94.94 **112.18**	42
6	5 to 7	1.9 **451**	1.4 **322**	5.6 **1,879**	0.2 **35**	1.479 **401.56**	77.84 **89.04**	30
12	11 to 13	1.7 **352**	1.2 **291**	4.4 **1,267**	0.2 **37**	1.174 **285.36**	69.06 **81.07**	30
18	15 to 21	1.9 **403**	1.8 **320**	6.2 **1,556**	0.0 **36**	1.378 **340.61**	72.53 **84.52**	30
24	23 to 25	2.6 **581**	2.0 **319**	9.6 **4,231**	0.4 **80**	1.939 **786.20**	74.58 **135.32**	30
30	29 to 31	2.7 **474**	2.4 **475**	6.4 **1,312**	0.4 **69**	1.424 **263.39**	52.74 **55.57**	30
36	34 to 38	2.5 **379**	2.0 **324**	7.8 **1,356**	0.0 **78**	1.714 **303.94**	68.56 **80.20**	30
48	46 to 50	3.1 **335**	2.6 **345**	10.4 **1,518**	0.2 **17**	2.295 **290.20**	74.03 **86.63**	30
5 days		3.9 **375**	3.2 **312**	11.0 **1,035**	1.2 **86**	2.491 **247.44**	62.27 **65.98**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

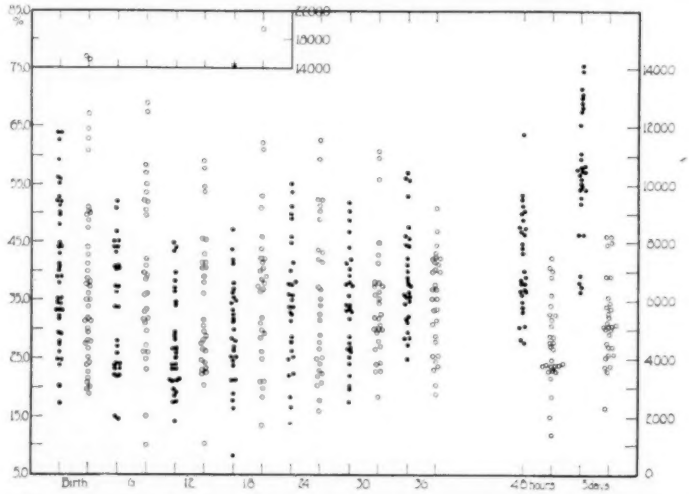

Fig. 17.—The distribution of absolute and percentage counts of medium lymphocytes. Solid dots, percentage counts; circles, absolute counts.

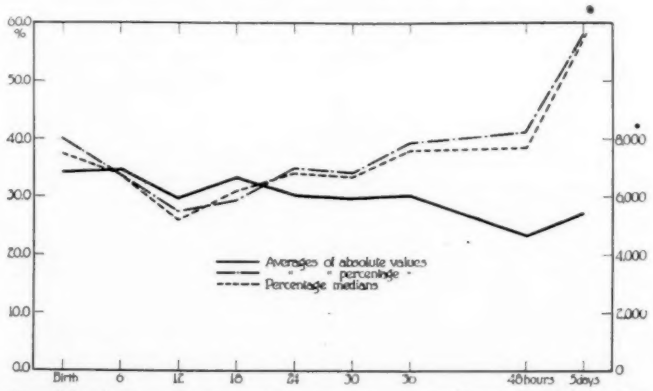

Fig. 18.—Absolute and percentage counts of medium sized lymphocytes.

TABLE 9.—*Absolute and Percentage Number of Medium Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	40.2 **6,841**	37.6 **6,278**	64.0 **15,392**	17.4 **2,896**	12.197 **3,148**	30.3 **46.01**	42
6	5 to 7	33.6 **6,921**	33.6 **6,753**	51.8 **12,864**	14.6 **1,081**	10.239 **2,871**	30.5 **41.49**	30
12	11 to 13	27.5 **5,967**	25.8 **5,358**	44.8 **10,841**	14.4 **1,012**	8.708 **2,380**	31.6 **39.88**	30
18	15 to 21	29.4 **6,635**	31.0 **6,665**	75.6 **19,504**	6.0 **1,764**	10.061 **2,385**	34.2 **35.64**	30
24	23 to 25	34.7 **6,063**	34.0 **5,880**	55.0 **11,615**	13.8 **2,691**	10.788 **2,568**	31.1 **42.22**	30
30	29 to 31	34.0 **5,984**	33.2 **5,525**	51.6 **11,248**	17.8 **2,775**	9.052 **2,034**	26.6 **33.99**	30
36	34 to 38	39.4 **6,018**	38.0 **6,423**	57.4 **7,996**	25.0 **2,856**	8.785 **1,567**	22.3 **26.04**	30
48	46 to 50	40.8 **4,634**	38.2 **4,593**	64.0 **7,568**	17.2 **1,462**	9.258 **1,434**	22.7 **30.94**	30
5 days		57.7 **5,459**	57.8 **5,220**	75.6 **8,321**	36.6 **2,457**	11.130 **1,434**	19.3 **26.26**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

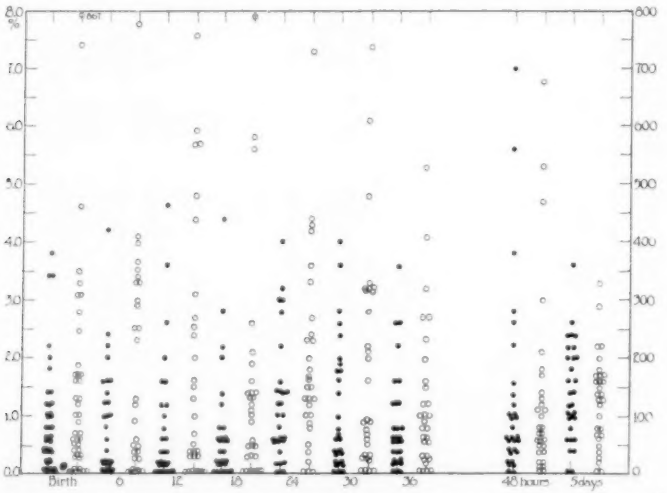

Fig. 19.—The distribution of absolute and percentage counts of large lymphocytes. Solid dots, percentage counts; circles, absolute counts.

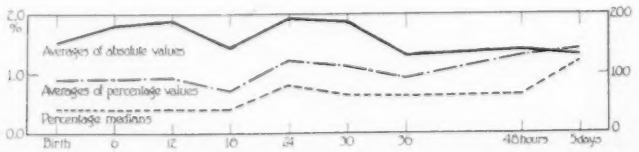

Fig. 20.—Absolute and percentage counts of large lymphocytes.

The medium lymphocytes usually form about from 85 to 90 per cent. of all the lymphocytes (Figs. 17 and 18 and Table 9, Figs. 19 and 20 and Table 10).

TABLE 10.—*Absolute and Percentage Number of Large Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.9 **151**	0.4 **91**	3.8 **867**	0.0 **0.0**	0.943 **184.86**	117.9 **122.42**	42
6	5 to 7	0.9 **179**	0.4 **121**	4.2 **777**	0.0 **0.0**	0.953 **183.74**	105.9 **102.65**	30
12	11 to 13	0.9 **189**	0.4 **108**	4.6 **759**	0.0 **0.0**	1.135 **215.92**	126.1 **114.24**	30
18	15 to 21	0.7 **141**	0.4 **100**	4.4 **792**	0.0 **0.0**	0.964 **184.76**	137.7 **131.04**	30
24	23 to 25	1.2 **193**	0.8 **151**	4.0 **729**	0.0 **0.0**	1.044 **160.10**	87.0 **82.95**	30
30	29 to 31	1.1 **187**	0.6 **96**	4.0 **738**	0.0 **0.0**	1.053 **176.59**	95.7 **94.43**	30
36	34 to 38	0.9 **128**	0.6 **99**	3.6 **530**	0.0 **0.0**	0.871 **125.91**	96.8 **98.37**	30
48	46 to 50	1.3 **137**	0.6 **87**	7.0 **679**	0.0 **0.0**	1.590 **158.96**	122.3 **116.03**	30
5 days		1.4 **131**	1.2 **140**	3.6 **331**	0.0 **0.0**	0.824 **77.75**	58.9 **59.35**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

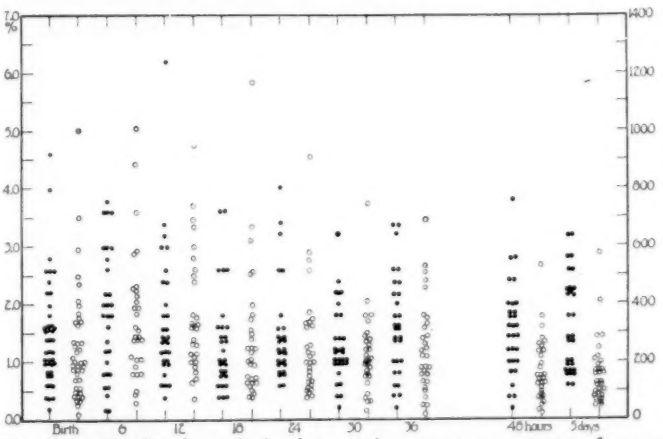

Fig. 21.—The distribution of absolute and percentage counts of mononuclear leukocytes. Solid dots, percentage counts; circles, absolute counts.

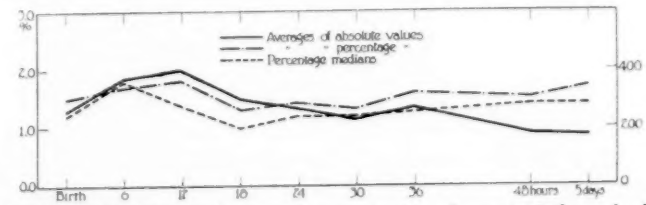

Fig. 22.—The absolute and percentage counts of mononuclear leukocytes.

(*e*) The Large Mononuclear Leukocytes: The curve of the large mononuclears is similar to that of the lymphocytes, and the variations at the various time intervals correspond closely to those of the total lymphocytes. The average of large mononuclears is usually about 1.5 per cent (Figs. 21 and 22 and Table 11).

TABLE 11.—*Absolute and Percentage Number of Large Mononuclear Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	1.5 **255**	1.2 **198**	4.6 **1,002**	0.2 **20**	0.911 **187.33**	60.73 **73.46**	42
6	5 to 7	1.7 **363**	1.8 **312**	3.8 **1,015**	0.2 **68**	0.905 **220.32**	53.24 **60.69**	30
12	11 to 13	1.8 **399**	1.4 **336**	3.4 **1,413**	0.4 **76**	1.153 **279.58**	64.06 **70.07**	30
18	15 to 21	1.3 **290**	1.0 **243**	3.6 **1,170**	0.4 **84**	0.793 **224.33**	61.00 **77.36**	30
24	23 to 25	1.4 **265**	1.2 **223**	4.0 **912**	0.6 **81**	0.836 **180.36**	59.71 **68.06**	30
30	29 to 31	1.3 **230**	1.2 **216**	3.1 **755**	0.2 **34**	0.655 **133.24**	50.38 **57.93**	30
36	34 to 38	1.6 **253**	1.6 **225**	3.4 **693**	0.2 **21**	0.842 **157.64**	52.62 **62.31**	30
48	46 to 50	1.5 **176**	1.4 **154**	3.8 **532**	0.2 **26**	0.781 **109.45**	52.07 **62.19**	30
5 days		1.7 **170**	1.4 **160**	3.2 **416**	0.6 **53**	0.818 **110.61**	48.12 **65.06**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

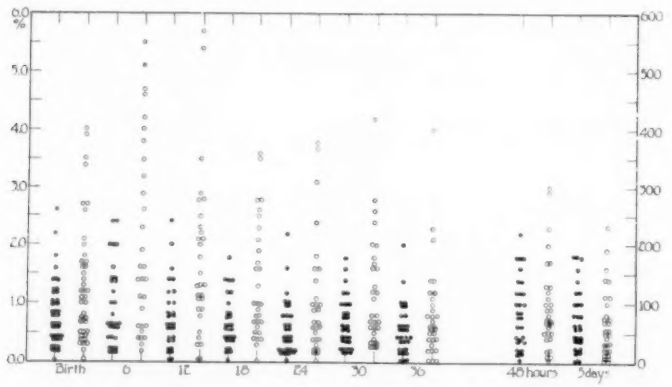

Fig. 23.—The distribution of the absolute and percentage counts of transitional leukocytes. Solid dots, percentage counts; circles, absolute counts.

(*f*) The Transitional Leukocytes: The transitionals are relatively uncommon. When the absolute values are plotted a curve results that closely resembles that of the P. M. N. neutrophils (Figs. 23 and 24 and Table 12).

(*g*) The Eosinophilic Leukocytes: The eosinophils, when plotted according to percentages, showed a very interesting curve. Immediately after birth there was a slight drop until twelve hours, followed by a continuous rise until forty-eight hours after birth. However, on plotting the absolute values it was seen that there was no true eosinophilia. The

count increases slowly until thirty hours and then decreases. This is a further argument against drawing conclusions from percentage values only (Figs. 25 and 26 and Table 13). The highest eosinophil percentage observed was 7.2. In exceptional instances no eosinophils were seen.

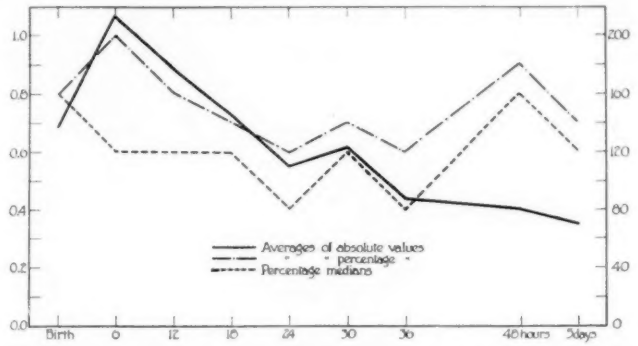

Fig. 24.—The absolute and percentage counts of transitional leukocytes.

TABLE 12.—*Absolute and Percentage Number of Transitional Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.8 **137**	0.8 **119**	2.6 **408**	0.0 **0.0**	0.547 **103.00**	68.4 **75.18**	42
6	5 to 7	1.0 **213**	0.6 **168**	2.4 **559**	0.2 **47**	0.678 **161.68**	67.8 **75.91**	30
12	11 to 13	0.8 **177**	0.6 **132**	2.4 **576**	0.0 **0.0**	0.556 **137.03**	69.5 **77.42**	30
18	15 to 21	0.7 **144**	0.6 **103**	1.8 **364**	0.0 **0.0**	0.435 **94.34**	62.1 **65.51**	30
24	23 to 25	0.6 **109**	0.4 **71**	2.2 **388**	0.0 **0.0**	0.447 **97.62**	74.5 **89.56**	30
30	29 to 31	0.7 **123**	0.6 **86**	1.8 **424**	0.2 **32**	0.424 **92.41**	60.6 **75.13**	30
36	34 to 38	0.6 **87**	0.4 **63**	2.0 **408**	0.0 **0.0**	0.424 **81.24**	70.7 **93.38**	30
48	46 to 50	0.9 **79**	0.8 **61**	2.2 **308**	0.0 **0.0**	0.583 **81.26**	64.8 **105.53**	30
5 days		0.7 **70**	0.6 **52**	1.8 **237**	0.0 **0.0**	0.519 **53.25**	74.1 **83.21**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

(*h*) The Eosinophilic Metamyelocytes: Eosinophilic metamyelocytes are rare. They are occasionally seen at from thirty to thirty-six hours after birth, when the number of eosinophils is greatest.

(*i*) The Eosinophilic Myelocytes: Eosinophilic myelocytes are still less frequent. Usually, when eosinophilic myelocytes are present, eosinophilic metamyelocytes can be found in the same smear.

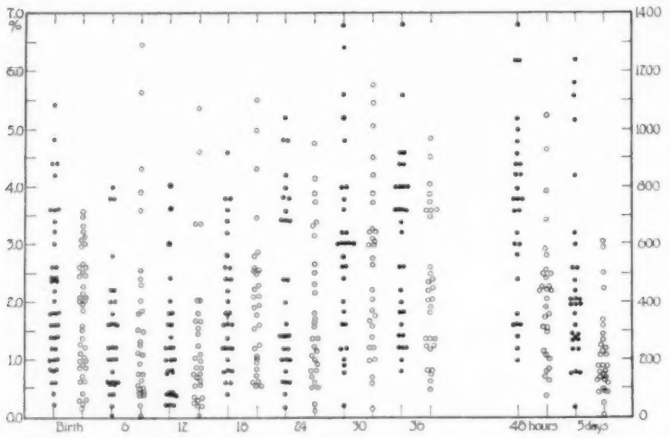

Fig. 25.—The distribution of the absolute and percentage counts of eosinophilic leukocytes. Solid dots, percentage counts; circles, absolute counts.

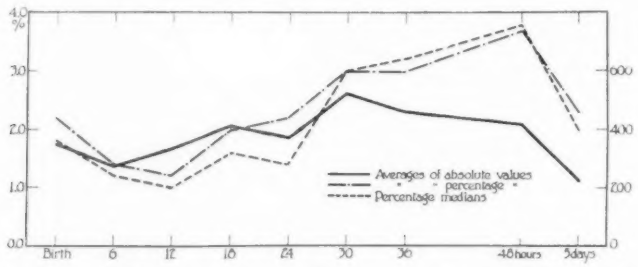

Fig. 26.—The absolute and percentage counts of eosinophilic leukocytes.

TABLE 13.—*Absolute and Percentage Number of Eosinophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	2.2 **356**	1.8 **392**	5.4 **716**	0.2 **37**	1.272 **199.21**	57.82 **55.96**	42
6	5 to 7	1.4 **272**	1.2 **192**	4.0 **1,076**	0.0 **0.0**	0.948 **304.50**	67.71 **92.27**	30
12	11 to 13	1.2 **330**	1.0 **256**	4.0 **1,292**	0.0 **40**	0.888 **254.62**	74.00 **93.61**	30
18	15 to 21	2.0 **410**	1.6 **393**	4.6 **1,108**	0.4 **110**	1.058 **251.26**	52.90 **61.28**	30
24	23 to 25	2.2 **371**	1.4 **319**	5.2 **955**	0.2 **29**	1.466 **253.24**	66.64 **68.26**	30
30	29 to 31	3.0 **525**	3.0 **553**	6.8 **1,152**	0.2 **30**	1.596 **289.97**	53.20 **55.23**	30
36	34 to 38	3.0 **462**	3.2 **448**	6.8 **975**	0.8 **126**	1.479 **247.49**	49.30 **53.57**	30
48	46 to 50	3.7 **419**	3.8 **442**	7.2 **1,051**	1.0 **89**	1.664 **228.68**	44.97 **54.58**	30
5 days		2.3 **221**	2.0 **182**	6.2 **616**	0.2 **13**	1.466 **148.01**	63.74 **66.97**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

(*j*) The Basophilic Leukocytes: Basophils are rarely seen in the blood of the new-born. At birth they are relatively numerous both in percentage and in absolute numbers. After birth they decrease (Figs. 27 and 28 and Table 14).

(*k*) The Rieder Cells: The Rieder cells are most numerous during the first twenty-four hours. Their numbers do not vary greatly

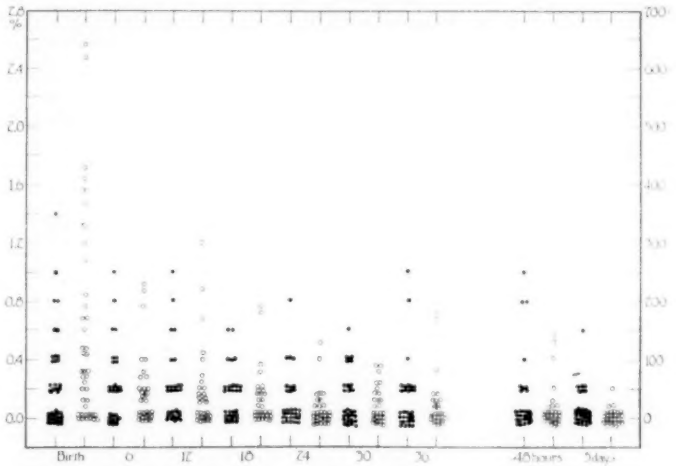

Fig. 27.—The distribution of the absolute and percentage counts of basophil leukocytes. Solid dots, percentage counts; circles, absolute counts.

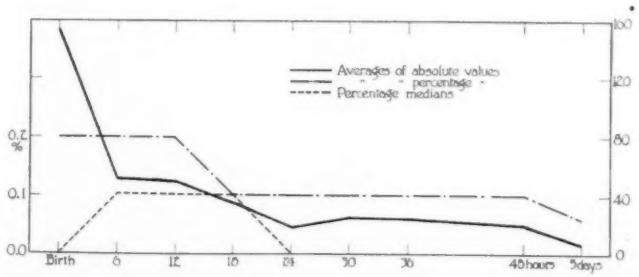

Fig. 28.—The absolute and percentage counts of basophil leukocytes.

and they seem to follow the curve of the lymphocytes. This is to be expected, since the Rieder cell seen in this study was limited to the lymphocyte type. At five days there is a slight increase in their frequency, corresponding to the increase in lymphocytes.

(*l*) The Plasma Cells: The plasma cells are infrequent. Their number is slightly greater during the first day and they show a definite rise at the five day period.

(*m*) The "Unusual" Cells: The so-called "unusual" cell, having the character of both a P. M. N. neutrophil and a promyelocyte, occurs occasionally during the first twenty-four hours but rarely after this period. It apparently is a cell that belongs to the neutrophil series and represents an irritation type. Occasionally more than one is seen in the same smear, and in one case five were seen.

(*n*) The Türke's Cell: The Türke's cell is rare. Two were seen during the first twelve hours. Both were present during markedly increased lymphatic activity.

TABLE 14.—*Absolute and Percentage Number of Basophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.2 **153**	0.0 **80**	1.8 **642**	0.0 **0.0**	0.300 **178.38**	1.50 **117.8**	42
6	5 to 7	0.2 **50**	0.2 **42**	1.0 **233**	0.0 **0.0**	0.244 **64.55**	1.22 **129.1**	30
12	11 to 13	0.2 **48**	0.2 **30**	1.0 **300**	0.0 **0.0**	0.244 **71.76**	1.22 **149.5**	30
18	15 to 21	0.1 **34**	0.2 **24**	0.6 **195**	0.0 **0.0**	0.173 **49.59**	1.73 **145.8**	30
24	23 to 25	0.1 **17**	0.0 **0.0**	0.8 **137**	0.0 **0.0**	0.173 **32.06**	1.73 **188.6**	30
30	29 to 31	0.1 **23**	0.0 **0.0**	0.6 **94**	0.0 **0.0**	0.173 **30.25**	1.73 **131.5**	30
36	34 to 38	0.1 **24**	0.0 **0.0**	1.0 **184**	0.0 **0.0**	0.223 **45.84**	2.23 **191.0**	30
48	46 to 50	0.1 **19**	0.0 **0.0**	1.0 **144**	0.0 **0.0**	0.264 **38.65**	2.64 **214.7**	30
5 days		0.06 **6**	0.0 **0.0**	0.6 **55**	0.0 **0.0**	0.100 **12.25**	1.00 **204.1**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

(*o*) The Degeneration Forms: Broken cells would probably be a more appropriate name for this type. These have been very briefly mentioned in the literature, and a few investigators state that destroyed cells are often seen in the blood smears of the new-born. In this study an attempt has been made to classify the different types.

In general, there is a tendency for the cell count to be high when the number of degeneration forms is high. The curve in Figure 29 illustrates the close relationship between the total degeneration count and the total white count, as shown in Figure 7. The curve taken by the degenerate lymphocytes (Figs. 30 and 31 and Table 15) is very similar to that of the total lymphocyte count. With one or two exceptions the same applies for the neutrophil degeneration forms (Figs. 32 and 33 and Table 16).

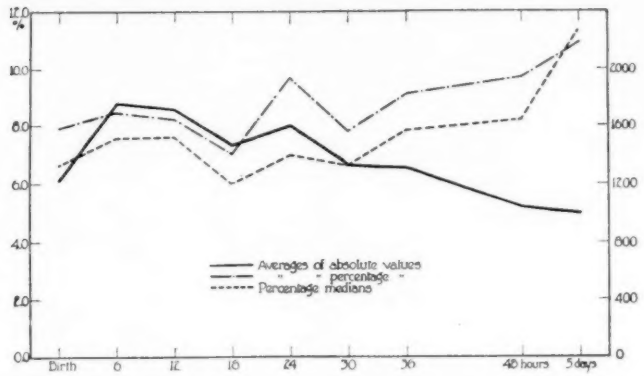

Fig. 29.—The absolute and percentage counts of all degenerating leukocytes.

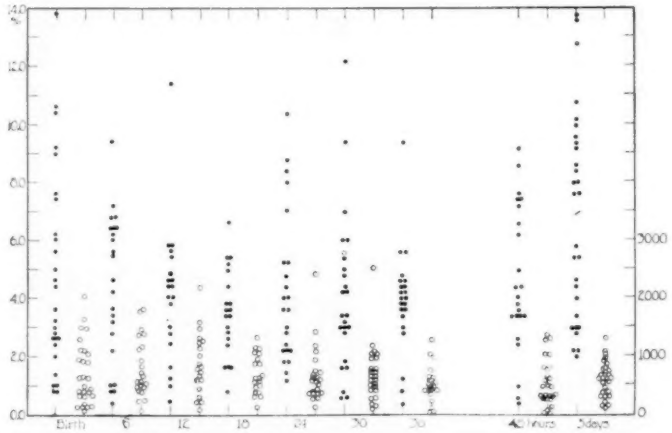

Fig. 30.—The distribution of the absolute and percentage counts of degenerating lymphocytes. Solid dots, percentage counts; circles, absolute counts.

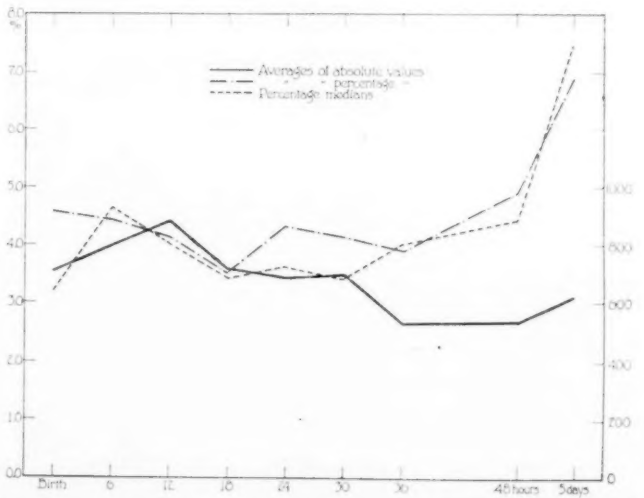

Fig. 31.—The absolute and percentage counts of degenerating lymphocytes.

TABLE 15.—*Absolute and Percentage Number of Degenerating Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	4.6 **709**	3.2 **612**	13.8 **2,014**	0.0 **110**	3.858 **521.02**	83.87 **73.49**	28
6	5 to 7	4.4 **792**	4.6 **604**	9.4 **1,849**	0.4 **50**	2.420 **548.14**	55.00 **69.78**	23
12	11 to 13	4.1 **878**	4.0 **777**	11.4 **2,188**	0.4 **82**	2.323 **506.98**	56.66 **57.74**	20
18	15 to 21	3.5 **706**	3.4 **588**	6.6 **1,325**	0.8 **144**	1.479 **323.11**	42.26 **45.77**	20
24	23 to 25	4.3 **687**	3.6 **600**	10.4 **2,412**	1.2 **135**	2.551 **478.92**	59.33 **69.71**	23
30	29 to 31	4.1 **692**	3.4 **615**	12.2 **2,513**	0.6 **103**	2.590 **466.48**	63.17 **67.41**	25
36	34 to 38	3.9 **530**	4.0 **507**	9.4 **1,269**	0.4 **54**	1.676 **288.92**	42.97 **54.51**	22
48	46 to 50	4.9 **540**	4.4 **494**	14.6 **1,324**	0.4 **46**	3.029 **358.94**	61.82 **66.47**	26
5 days		6.9 **620**	7.6 **621**	13.8 **1,346**	2.0 **162**	3.534 **284.44**	51.22 **45.88**	29

* The upper figures represent percentage counts; the figures in bold face, the total counts.

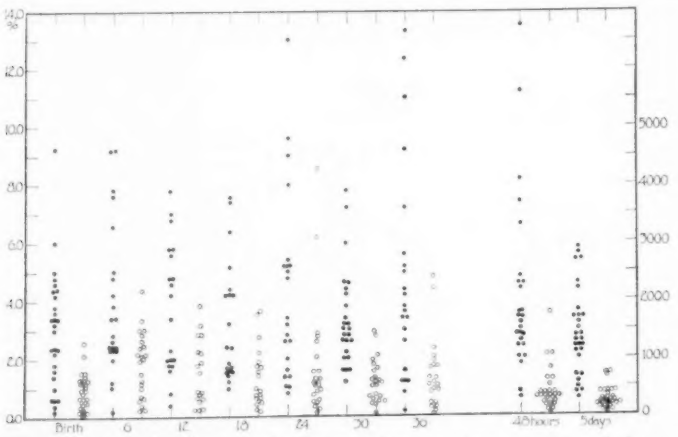

Fig. 32.—The distribution of absolute and percentage counts of degenerating neutrophilic leukocytes. Solid dots, percentage counts; circles, absolute counts.

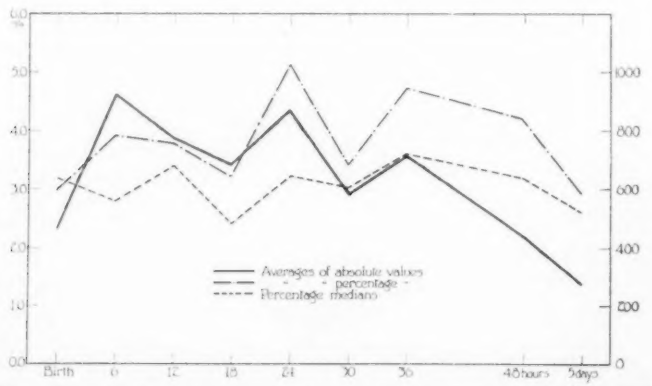

Fig. 33.—The absolute and percentage counts of degenerating neutrophilic leukocytes.

TABLE 16.—*Absolute and Percentage Number of Degenerated Neutrophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.0 **460**	3.2 **414**	9.2 **1,269**	0.2 **35**	1.959 **298.17**	65.3 **64.8**	28
6	5 to 7	3.9 **917**	2.8 **1,036**	9.2 **2,190**	0.2 **100**	2.501 **480.51**	64.1 **60.7**	23
12	11 to 13	3.8 **769**	3.4 **782**	7.8 **1,938**	0.4 **123**	2.179 **547.44**	57.3 **71.2**	20
18	15 to 21	3.2 **677**	2.4 **424**	7.6 **1,831**	1.0 **108**	2.128 **504.57**	66.5 **74.6**	20
24	23 to 25	5.1 **865**	3.2 **598**	23.0 **4,278**	0.8 **75**	4.919 **956.39**	96.5 **110.6**	23
30	29 to 31	3.4 **582**	3.0 **516**	7.8 **1,483**	1.2 **45**	1.685 **353.97**	45.5 **60.8**	25
36	34 to 38	4.7 **708**	3.6 **589**	13.4 **2,430**	0.2 **28**	3.674 **601.42**	78.2 **85.0**	22
48	46 to 50	4.2 **438**	3.2 **316**	13.6 **1,768**	0.6 **40**	2.969 **368.10**	70.7 **84.0**	26
5 days		2.9 **274**	2.6 **246**	5.8 **739**	0.6 **55**	1.466 **176.97**	50.6 **64.6**	29

* The upper figures represent percentage counts; the figures in bold face, the total counts.

In the case of the eosinophils, however, the curves of the total count of degeneration forms and the total number of normal cells do not

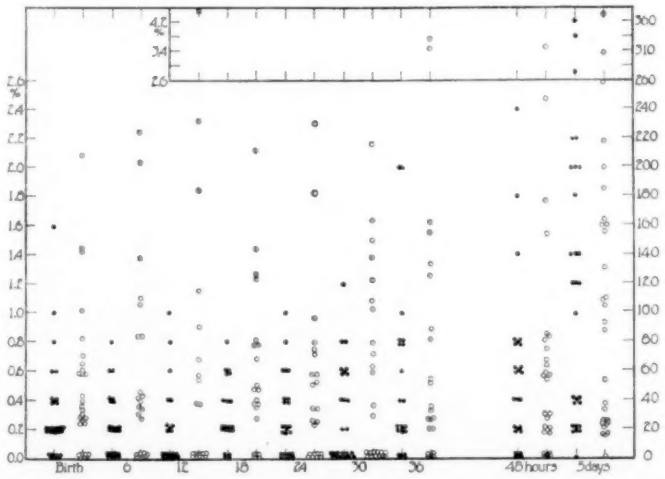

Fig. 34.—The distribution of absolute and percentage counts of degenerating eosinophilic leukocytes. Solid dots, percentage counts; circles, absolute counts.

correspond. As will be seen in Figures 34 and 35 and Table 17, the eosinophil degeneration is greatest at five days. There seems to be a gradual tendency toward increased degeneration throughout the period.

(*p*) The Nucleated Red Blood Cells: Figures 36 and 37 and Table 18 show the incidence of the nucleated red blood cells. The number is greatest at birth, but between birth and eighteen hours there is a sudden decrease. The curve then flattens out until thirty hours and is followed by a gradual decrease for five days, when only one nucleated red cell was seen in the entire thirty cases.

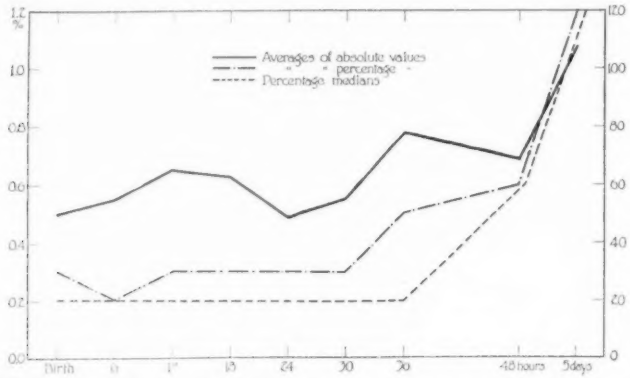

Fig. 35.—The absolute and percentage counts of degenerating eosinophilic leukocytes.

TABLE 17.—*Absolute and Percentage Number of Degenerated Eosinophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.3 **49**	0.2 **37**	1.6 **208**	0.0 **0.0**	0.346 **50.33**	115.3 **102.7**	28
6	5 to 7	0.2 **54**	0.2 **36**	0.8 **224**	0.0 **0.0**	0.223 **63.24**	111.5 **117.1**	23
12	11 to 13	0.3 **64**	0.2 **37**	1.0 **384**	0.0 **0.0**	0.479 **99.49**	159.7 **155.5**	20
18	15 to 21	0.3 **62**	0.2 **48**	0.8 **212**	0.0 **0.0**	0.223 **53.57**	74.3 **86.4**	20
24	23 to 25	0.3 **48**	0.2 **34**	1.0 **230**	0.0 **0.0**	0.264 **57.90**	88.0 **120.6**	23
30	29 to 31	0.3 **54**	0.2 **30**	1.2 **216**	0.0 **0.0**	0.331 **63.86**	110.3 **118.3**	25
36	34 to 38	0.5 **77**	0.2 **36**	2.0 **330**	0.0 **0.0**	0.565 **92.30**	113.0 **119.9**	22
48	46 to 50	0.6 **68**	0.6 **57**	2.5 **316**	0.0 **0.0**	0.663 **76.24**	110.5 **112.1**	26
5 days		1.2 **108**	1.2 **93**	4.2 **373**	0.0 **0.0**	1.086 **95.22**	90.5 **88.2**	29

* The upper figures represent percentage counts; the figures in bold face, the total counts.

In general, the nucleated red cells are slightly larger than the normal erythrocytes. Practically all are polychromatophilic, i. e., they belong to Group II or IV. Nucleated cells of Type I and III, i. e., with red cytoplasm, usually appear when large numbers of nucleated red cells are present. In these cases the large forms of nucleated red blood cells are also quite commonly seen.

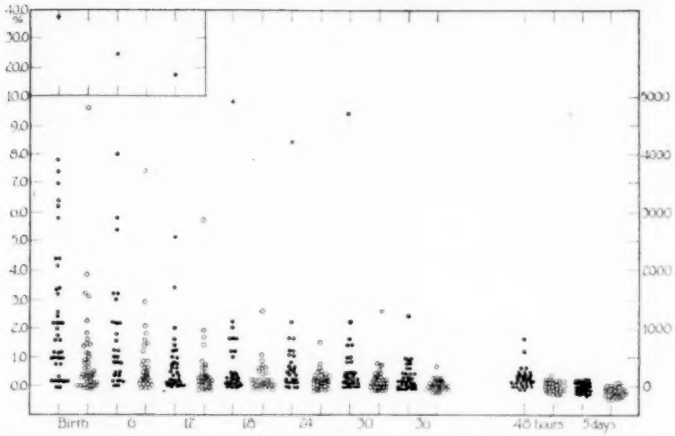

Fig. 36.—The distribution of the absolute and percentage counts of nucleated red blood corpuscles. Solid dots, percentage counts; circles, absolute counts.

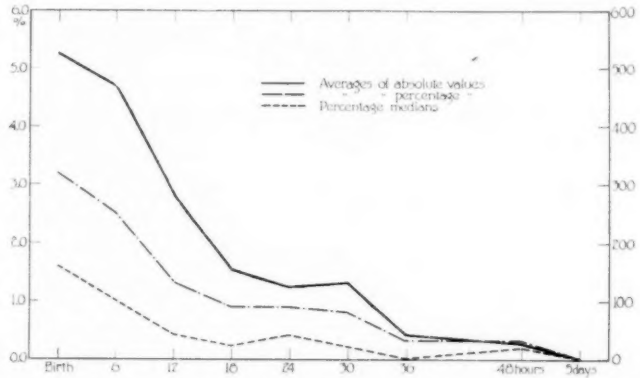

Fig. 37.—The absolute and percentage counts of nucleated red blood cells.

TABLE 18.—*Nucleated Red Blood Corpuscles Per 100 White Blood Corpuscles and Per Cubic Millimeter*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.2	1.6	37.8	0.0	5.818	181.81	42
		523	**492**	**4,800**	**0.0**	**665.82**	**127.3**	
6	5 to 7	2.5	1.0	24.4	0.0	12.715	508.6	30
		469	**250**	**3,708**	**0.0**	**697.57**	**148.7**	
12	11 to 13	1.3	0.4	17.8	0.0	3.249	249.9	30
		277	**70**	**2,883**	**0.0**	**546.02**	**197.1**	
18	15 to 21 †	0.9	0.2	9.8	0.0	1.783	198.1	30
		152	**48**	**1,274**	**0.0**	**249.31**	**164.0**	
24	23 to 25	0.9	0.4	8.4	0.0	1.506	167.3	30
		122	**46**	**756**	**0.0**	**151.41**	**124.1**	
30	29 to 31	0.8	0.2	9.4	0.0	1.700	212.5	30
		130	**43**	**1,616**	**0.0**	**292.92**	**225.3**	
36	34 to 38 †	0.3	0.0	2.4	0.0	0.469	156.3	30
		39	**0**	**324**	**0.0**	**66.89**	**171.5**	
48	46 to 50 †	0.3	0.2	1.6	0.0	0.360	120.0	30
		26	**14**	**152**	**0.0**	**36.45**	**140.2**	
5 days		0.0	0.0	0.2	0.0			
		0	**0**	**22**	**0.0**			

* The upper figures represent percentage counts; the figures in bold face, the total counts.
† 15 to 21 hours, only one case at 15 and one at 21 hours; 34 to 38 hours, only one case at 34 and one at 38 hours; 46 to 50 hours, two cases at 46 and two at 50 hours.

In only one case were there no nucleated red cells encountered at birth. In this instance one nucleated red cell was seen in a smear taken thirteen hours after birth, one at twenty-five hours and none at thirty-six or fifty hours.

Apparently the amount of polychromatophilia varies directly with the number of nucleated red cells. Thus in Case 4, in which no nucleated red blood cells were noted at 6, 12, 18 and 31 hours, there was little polychromatophilia until at forty-six hours when it became definitely noticeable, and two nucleated red cells were observed.

Case 25 was very unusual. At birth there were 37.8 nucleated red cells for every 100 leukocytes. This infant was born at term and weighed 3,690 gm. (8 pounds). After birth the number of nucleated red cells decreased rapidly and at thirty hours there were 9.4 for every 100 leukocytes. No nucleated red cells were present in the blood smears at five days. Other evidences of an increased red cell production were present. There were many naked erythroblast nuclei (Fig. 1 *r*), and all sizes of nucleated red cells including microblasts and megaloblasts. Mitotic figures were present at seven and eleven hours. The nuclei of many of the red cells were divided into three or four lobes and some contained Howell-Jolly bodies. No basophilic punctation could be found. Despite all the evidence of increased erythrogenesis in this case, the red count remained comparatively low, being below five million per cubic millimeter, except in one instance when it reached five million.

Apparently red cell formation does not vary with neutrophil production. Very often when there is evidence of hyperactivity of the red cells, the reverse is true of the neutrophils.

The shadows of red blood cells are not more commonly seen in new-born blood than in that of the normal adult.

As previously noted by other observers, rouleaux formation is not as active in new-born as in adult blood.

Polychromatophilia is as common in the average sized red cell as in the larger ones. The degree of polychromatophilia is quite variable (Fig. 1 *s*).

Poikilocytosis was observed repeatedly. Unlike the large pear-shaped cells seen in severe anemias, these cells are small and often pale (Fig. 1 *s*). In addition, one often sees small irregular red masses which seem to be detached portions of other red cells. The smallest microcytes are present in new-born blood, especially when red cell production is hyperactive.

Anisocytosis, which is seen in every smear, persists definitely at five days. At this time poikilocytosis and polychromatophilia are rare.

(*q*) Platelets: As a rule the platelets seem more variable in size than those seen in the adult, and forms larger than normal are rather common (Fig. 1 *t*). The granulation was in no way peculiar.

5. *The Leukocyte Granules.*—The neutrophilic and eosinophilic granules are similar to those of the normal adult in every respect. The azure granulation tends to be less abundant than in the normal adult. However, the variations are similar, so that on one day the granules may be abundant, while on the next they may be scanty.

6. *Icterus Neonatorum.*—In this work it was possible, by examining the blood at different intervals, to determine whether blood changes took place during the development of marked icterus. In the few cases of marked icterus the blood showed no abnormalities. One case showed a very low eosinophil count, 0.2 per cent. at six days, but in the other cases the eosinophils were normal.

7. *Sex Differences.*—No difference in the blood findings of newborn males and females were noted in the present study.

8. *Numerical and Graphical Results.*—Although a very large number of individual and serial counts of the various types of blood cells for all periods of postnatal life have been published, the only attempts to estimate the variability of these counts were given in the form of estimates of the range, as indicated by the maxima and minima. While the range is one of the commonest measures of deviation used in the study of variable observations, it is perhaps the least valuable of all the measures which have been devised for the purpose. Among the objections which may be raised to its exclusive use are the following: First, it is dependent on two observations only, the largest and smallest of the series, and it can be no more accurate than these observations; Second, it is little influenced by the number of observations in the series, the range on 200 cases being as liable to vary as the range in a series of two cases. Third, it gives no concept of the relation of the individual observations to the average of these observations, for the maximal and minimal observations may be far removed from the average, while the great majority of the observations are closely clustered about the average. It seems highly desirable that modern measures of dispersion should be applied to blood counts at all ages, since the variations in these counts are used constantly for differentiating the normal from the abnormal, as well as for the study of changes under different physiologic conditions.

The study of the variability of the various blood counts in the newborn has been carried out by the computation of the standard deviation and the coefficients of variability, as explained in the section on statistical methods in the foregoing part of this paper. In the present section, a brief summary will be given of the results obtained with these methods.

The variability of the red blood corpuscles was determined on the basis of a unit of 10,000 cells, since the original counts were made to this figure. The deviations of the various individual counts from the median and average are shown in Figure 3, and the calculated deviations are fairly symmetrical, as shown by the close relation of the median to the average count. The average range of the cases is about 2.5 million. The range seems to be greater in the middle of the period of observation than at the beginning or at the end. The standard deviation ranges from about 500,000 to about 750,000. It is greatest between the sixth and twenty-fourth hours. Taken as a whole, the coefficient of variability of the red blood cell count is remarkably small and very constant. It averages about 11 per cent. How constant the red blood count of the new-born really is may be shown by comparing its coefficient of variability with that of some other measures in the new-born; thus the variability in height at birth is about 6 per cent., the variability in weight is about 15 per cent., while the variability in weight of the thymus is 47 per cent., and that of the weight of the thyroid is 53 per cent. There is no evidence that the coefficient of variability of the red cell count changes with the increase in this count in the course of the first day.

In contrast to the red blood cells, the blood platelet count is very variable. The range between the maximal and minimal counts runs between 200,000 and 400,000. The distribution of the cases tends toward the minimum, as is indicated by a median which is always lower than the arithmetic average. The standard of deviation averages about 65,000 and the coefficient of variability ranges from 46.1 to 28.5 per cent. There is a very distinct drop in the variability after the first day.

While the variability of the total white cell count is relatively larger than that of the red cell count, it is fairly constant when one considers the different factors which may affect it. The range of variation, however, is very great, being over 10,000. On the average, the standard deviation varies from 5.26 thousand at thirty hours to 2.52 thousand on the fifth day. The coefficient of variability is about 25 per cent. of the average. It is greatest at birth, but from six hours on throughout the period of observation it is quite constant.

The variability of the absolute counts of the various types of white blood cells differs greatly with the several varieties.

The polymorphonuclear leukocytes have an average range of over 15,000, and the average of the standard deviations is, in round numbers, about 3,000. The coefficient of variability is about 35 per cent. of the average count. Thus the polymorphonuclear leukocyte count is about one-third more variable than that of the total white cell count. There is no consistant change in the variability of the total absolute number of the polymorphonuclear leukocytes during the period of observation.

The range in total number of the lymphocyte cells averages about 7,000, and the standard deviation declines from about 3,500 at birth to about 1,500 at the end of the period of observation. The coefficient of variability ranges from 46.5 at birth to 25.0 per cent. at five days after birth. Both the standard deviation and the coefficient of variability drop steadily and consistently after the first day, although there is only a slight decrease in the actual count of lymphocytes in this period.

The changes in the variability of the medium sized lymphocytes is practically the same as that in the entire lymphocyte group, since they form the greater part of this group.

Both the large and the small lymphocytes show the greatest variability. In the case of the former the coefficient of variability ranges from 122.4 per cent. at birth to 59.3 per cent. at five days. In the latter, the coefficient of variability shows no constant change except that it is lower on the fifth day than earlier.

The range of the absolute number of large mononuclear leukocytes is extremely great, being on the average about 1,000, while the average absolute count is about 250. It shows no great or consistent change during the period of observation.

The variation of the transitional leukocytes is slightly greater than that of the large mononuclears, but like the latter shows no constant changes.

The eosinophil leukocytes are less variable than most of the cells which occur in small numbers in the circulating blood. While the range of variation is great, considering the small absolute number of cells, the coefficient of variability ranges from about 94 to 53 per cent. The variability is higher the first day than later.

The basophil leukocytes are the most variable of all the blood cells. The range of distribution is commonly about four times the average count in the period of observation, and the coefficient of variability has a minimum of 117.2 at birth and a maximum of 214.7 on the second day. Unlike most of the other cell counts the basophils become much more variable in the latter part of the period of observation.

The variability of the degenerated forms of leukocytes is not as great as might be expected from the nature of the material. The degenerated neutrophil leukocytes show an average coefficient of variability of about 80 per cent. At the end and the beginning of the period the coefficient is but little over 60 per cent., but it rises to over 100 per cent. at the end of the first day. The coefficient of variability of the degenerated eosinophils is higher than that of the neutrophils, averaging over 100 per cent. It is extremely irregular in the different intervals of observation.

The degenerating neutrophils show an average coefficient of variability of about 85 per cent. with no constant change.

The degenerating eosinophils show even a higher coefficient of variability, averaging about 90 per cent. The variability is quite irregular in the period of observation.

The variability of the degenerating lymphocytes is somewhat less, being about 60 per cent. It is higher at birth than at any other time in the period of observation.

The variability of the nucleated red corpuscles is very great. It ranges from 120 to 508 per cent. It shows no constancy at the various times of observation.

The percentage counts of the various leukocytes, taken as a whole, are much less variable than the absolute counts. The average coefficient of variability of the number of these cells is approximately 20 per cent. It shows no constant change during the period of observation. The variability of the number of lymphocytes is slightly greater than that of the polymorphonuclear leukocytes, averaging about 22 per cent. There is a distinct decrease in the variability after the first day. The variability of the large and small lymphocytes is very great, the coefficient of variability of the percentage count being almost or quite equal to that of the absolute count. The coefficient of variability of the large mononuclear lymphocytes averages about 55 per cent. The variability decreases somewhat after the first day. The coefficient of variability of the transitional leukocytes is somewhat greater than the large mononuclears, being between 65 and 70 per cent. The variability shows no consistent change during the period of observation. The count of the eosinophils shows an average coefficient of variability of about 55 per cent. It shows no constant change in the period. The percentage count of the basophils, like the absolute number of these cells, is tremendously variable. The average coefficient is approximately 170 per cent. Like the variability of the absolute numbers, the variability of the percentage count tends to increase during the new-born period. The coefficient of variability of the absolute number of lymphocytes is about 55 per cent. It is lower in the latter part of the period of observation than in the earlier. The absolute number of nucleated red blood corpuscles is extremely variable. The coefficient ranges from 127 on the first day to 225 per cent. at thirty hours.

COMMENT

1. *The Red Blood Cell Count.*—The rapid rise in the erythrocyte count during the first six hours explains the types of red cells observed. At this stage, nucleated red cells, polychromatophilia, anicocytosis and poikilocytosis are most frequently seen. After this initial stimulation the number of red blood cells decreases and tends to become fairly constant. If blood concentration is responsible for this rise in cell count,

surely the small intake of fluid between six and eighteen hours cannot restore conditions to normal. An analysis of our material shows definitely that the amount of weight loss in the first two days bears no relationship to the red cell count. Many of our cases were given complementary feedings of breast milk or lactose solution in an attempt to prevent the initial drop of weight. We were fortunate in obtaining several infants in whom the weight loss was very small. In these infants there was apparently very little concentration, and yet the rise in the red blood cell count was present. In only eight of the thirty-five cases studied, did the curves show an increase in red cells corresponding to the weight loss, while in fifteen cases the reverse was true.

At birth, the excretions are already formed in the bowel and bladder, and any concentration as a result of these excretions has already taken place. Further concentration would only occur if more of the excretions were rapidly formed, which is not the case in the first twelve hours. The amount of moisture lost in respiration during the first six hours apparently does not exceed that lost during the next twelve hours, so that there should be little change in blood concentration at different periods during the first eighteen hours because of fluid lost in respiration.

As will be shown later, the bone marrow is exceedingly active during the first few hours after birth, and this is probably an important factor in causing the initial rise in red cell count. Stimulation of any organ may be temporary, especially immediately after birth when such marked changes occur in the infant's organism.

It would be interesting to determine the blood volume of the newborn at the intervals studied in this work and to compare the results with our figures, for then one could state with absolute certainty whether or not concentration is a factor that helps to account for the initial increase of red blood cells.

2. *The Platelet Count.*—It is surprising that the neonatal rise, which is characteristic of the red and white cells, does not occur in the platelets; on the contrary the number begins to decline directly after birth. Lucas and his co-workers found no count less than 100,000, but in our series there were a few below this figure.

3. *The Leukocyte Count.*—The rapid rise and fall of the white cell count seems to be very uniform. The flattening of the curve between twenty-four and thirty hours is apparently due to the few unusually low counts at twenty-four hours. From forty-eight hours to five days the drop is slower. After the five day period other observers have found that the white count remains about from 7,000 to 10,000. This is mentioned chiefly because one often reads that increased leukocyte counts of 12,000 to 15,000 are normal values for infants and children.

4. *The Differential Leukocyte Count.*—The close relationship of the total leukocyte count to that of the polymorphonuclears indicates that the changing number of the latter is chiefly responsible for the variation in the white blood count during the first two days.

The metamyelocytes are irritation types of cells. In the normal differential count one may find one or two metamyelocytes in every 100 cells. In cases of leukocytosis as the result of inflammation, which we know is an expression of increased bone marrow activity, many metamyelocytes are seen. It is logical to assume, therefore, from the curve of the metamyelocytes that the bone marrow is in a state of hyperactivity during the first twelve to eighteen hours. In order to obtain a satisfactory idea of the neutrophilic components of the blood stream, it is necessary to add the values obtained for the neutrophilic metamyelocytes and polymorphonuclears.

The presence of neutrophilic myelocytes is another indication of stimulation of bone marrow activity. According to Pappenheim, one finds metamyelocytes and myelocytes in cases of bone marrow irritation, as in reaction to hemorrhage. Cells earlier than myelocytes occur only in pathologic reaction of the bone marrow.

The lymphocyte curve shows several points of interest. The literature contains a number of such curves representing percentage counts, and these indicate that during the first few days the number of lymphocytes gradually increases. That this is not the case is shown by the curve of the absolute number of cells.

When one studies the lymphocytes in the first twelve to eighteen hours, it is seen that here too, there are evidences of increased activity of lymphocyte production. For example, one sees earlier types of lymphocytes, cells with sieve-like nuclear structure. Other evidences of lymphocyte irritation will be shown later. When the number of total lymphocytes is high, one usually finds that the increase in the small and large forms is relatively greater than the increase of medium sized cells.

In this study, the absolute values of lymphocytes and polymorphonuclears were found to be equal at forty-eight hours, and after this period the lymphocytes were more numerous than the neutrophils. Practically all other observers have found that this change occurs between the fourth and sixth days.

The values of the mononuclears and transitionals closely approximate those of the normal adult. No cases were met in which the number of either of these cells was unusually high.

It is difficult to say whether any significance can be attached to the elevation in the number of eosinophils at thirty hours, but one infers that the eosinophil production is increased at this time since the total leukocyte count has dropped definitely at thirty hours.

In several of the smears eosinophils were noted in which the eosinophilic granules were embedded in a blue cytoplasm. Ordinarily, the cytoplasm consists entirely of these large coarse granules, the blue cytoplasm being present only in the earlier stages of eosinophil formation. This has been shown to be the case by Downey [37] in a study of eosinophil production in the marrow of the guinea-pig. It is possible that the same changes do not occur in man.

The presence of eosinophilic metamyelocytes and myelocytes is another evidence of bone marrow hyperactivity. Both are rarely seen; the metamyelocytes are more numerous.

As others have shown basophils are rare in new-born blood, but there seems to be no previous record that the incidence is higher at birth. Although the numbers dealt with are small, still at birth there are three times as many basophils present as at twelve hours.

The Rieder cell is a distinct irritation type of cell seen only in increased hemopoietic activity. The lymphocytic type is more commonly met than the myeloid type and is frequently seen in Hodgkin's disease, lymphosarcoma and lymphatic leukemia. Its presence in this study is definite evidence of increased blood cell production.

Plasma cells are rarely seen in blood smears except when there is either lymphatic hyperactivity, or in chronic infectious diseases. The close relationship between lymphocyte and plasma cell formation has been definitely established.

The "unusual" cell or promyelocyte type is another evidence of a hyperactive blood forming mechanism. At first sight it seemed that this cell was typical of new-born blood, but later studies indicate that this is not the case.

Apparently no systematic study has previously been made of degeneration forms in human blood. It was found that these cells could be classified in groups and their curves of incidence determined. The close relationship between the total number of leukocytes and the number of degeneration forms suggests that they are more vulnerable during periods of the increased production of cells. One often sees degenerating lymphocytes in lymphatic leukemia and occasionally when lymphatic hyperplasia occurs, as in Hodgkin's disease. Apparently in these cases also, vulnerable cells are formed with rapid production.

Some cases show the tendency to produce more degenerate forms than others. In a few cases the number of degenerate forms at each successive time interval was increased.

Pressure in making the smears cannot be the cause of the increased degeneration in the first twelve hours, for the same technic was used at

37. Downey, H.: The Origin and Development of Eosinophil Leukocytes and of Haematogenous Mast Cells in the Bone Marrow of Adult Guinea-Pig, Folia Haematol. **19**:148, 1915.

twelve hours as at five days, and unless the cells happened to be less resistant at twelve hours, there should be equal numbers of degenerate forms at both intervals. Furthermore, when studying the smears, one often sees several intact cells in the midst of a group of degeneration forms. Apparently the area under observation had been subjected to the same pressure throughout, and these cells, which were more vulnerable for a cause not specifically known, were more easily crushed.

As has been previously mentioned the eosinophil degeneration continues to increase from forty-eight hours to five days. The increase seen between forty-eight hours and five days corresponds to the increase in eosinophil count during the same period (Fig. 26). Apparently the vulnerability of the eosinophils occurs later than does that of the neutrophils and lymphocytes.

In a previous research on azure granulation,[38] an experiment was performed in which citrated blood was allowed to stand in a test tube on ice for several days. Smears were made every day, and it was noted that the eosinophils remained intact much longer than did the neutrophils and lymphocytes. In one case in the present study (Case 38 F) there were at five days nineteen degenerated eosinophils, ten degenerated neutrophils and ten degenerated lymphocytes to every 500 normal leukocytes. When one considers that the eosinophils formed but 6.2 per cent. of the total number of cells it is apparent that the degeneration was due to an increased vulnerability of that particular cell.

Nucleated red blood cells were found in every case studied. The total number does not increase from birth to twelve hours, as do most of the leukocytes.

The case cited in which the new-born had 37.8 per cent. nucleated red blood cells is very striking. One would think that either the marked reaction was pathologic or that prematurity was the causative factor. However, the child was definitely mature, and there was no clinical evidence present indicating any abnormality. The low erythrocyte count in the case suggests that an attempt was being made to produce red cells for the physiologic need.

The work of Drinker and Lund [39] helps to throw some light on our problem. They found in their perfusion experiments that when normal bone marrow is perfused under pressure, the marrow remains intact. When, however, the bone marrow is hyperactive and is sending out nucleated red blood cells, an increase of the blood supply will cause an increase in the number of nucleated red blood cells forced out into the circulation. It is very likely that the great variations observed in the

38. Lippman, H. S.: A Comparative Study of Azure Granules Under Normal and Pathological Conditions, Mss., M. A. Thesis, University of Minnesota, 1920.

39. Drinker, C. K.; Drinker, K. R., and Lund, C. C.: Circulation in Mammalian Bone Marrow, Am. J. Physiol. **62**:1 (Sept.) 1922

numbers of nucleated red blood cells in our study were due to differences in the blood volumes of the new-born. Incidentally, early forms of lymphocytes and neutrophils are present in the case under discussion, so that in all likelihood the blood picture represents a normal new-born with an extremely hyperactive hemopoietic system.

In most instances, no direct relationship exists between red cell and neutrophil cell formation. In fact, in numerous instances when red cell activity is markedly increased the neutrophil production is diminished.

The presence of megaloblasts and mitotic figures is indisputable evidence of an hyperactive bone marrow. In no case was basophilic stippling observed.

Taken as a whole, the red cell picture resembles that of secondary anemia following hemorrhage where one sees anisocytosis, polychromatophilia and nucleated reds. However, there is nothing present in the picture of the new-born blood to suggest anything but a physiologic process.

5. *The Leukocyte Granules.*—There is nothing unusual in the neutrophilic and eosinophilic granulation. The azure granules seem to be definitely reduced. The arrangements of the granules were found to be varied. Only a few of the smears contained cells with large coarse granules arranged in clumps and rows. They tend to be few in number, and medium or fine in size.

6. *The Causes of the Leukocytosis of the New-Born.*—In this series, infants whose delivery was attended by severe trauma showed leukocyte counts which corresponded closely to the averages for the entire group, so it does not seem probable that trauma is a factor in causing the leukocytosis of the new-born.

The theory of the causation of the natal leukocytosis through the peripheral stagnation of blood in the capillaries is not supported by this set of observations. The various components of the blood should all be quite similarly affected if the changes were simply due to a stagnation of cells. As a matter of fact, there is little relationship in each individual case between the number of red cells, platelets and leukocytes at the different time intervals. Again, the differential count should remain about the same at the various periods and this is not the case. The neutrophil reaction has been shown to be the cause of the fluctuating white cell count in the new-born child, the lymphocytes showing little change.

The concentration theory has been previously discussed. No special study was made of the effect of protein digestion on the new-born blood, but so far as could be determined the changes in the leukocyte count exhibited no relationship to the food ingested. The amount of food ingested during the first forty-eight hours is very slight, and the interval

between feedings is too short to determine the effect of protein digestion with accuracy.

There are many facts that cannot be satisfactorily explained on the theory that the condition of the blood of the new-born is a result of the continuation of fetal blood formation. One cannot account for the rise in blood elements at twelve hours, for the high values, if due to fetal activity, should be present at birth, but this is not characteristic of the blood at birth. The morphology of the blood at birth approximates that of the last part of fetal life, and the picture presented is far different from that seen at six hours and again at twelve hours.

On the whole, the observations reported in this study support the view that the neonatal changes in the morphology of the blood are due to the increased stimulation of the blood forming organs, rather than to any of the factors just discussed.

SUMMARY

1. The morphology of the blood of the new-born differs in many respects from that of the adult. The present study was undertaken to fill a gap in the knowledge of new-born blood during the first forty-eight hours after birth. So many changes occur at this time that a careful analysis of these variations is essential. The forty-eight hour period, therefore, has been divided into eight parts, thirty cases being included in each interval. Counts were made of the red blood cells, leukocytes and platelets. Differential studies included the examination of 500 cells in each blood smear. White counts and differential studies were again made at five days, to secure a further check on the material.

2. The red blood cells at birth average 5.2 million per cubic millimeter. During the first six hours the count rises to 5.6 million. Following this there is a drop to 5.4 million at eighteen hours, after which time the count remains fairly constant until forty-eight hours after birth.

3. The platelet counts at birth average 213,000 per cubic millimeter. It drops to 170,000 during the first six hours. The decrease continues until 18 hours after birth and is then followed by a slight increase. No changes from normal were observed in the platelet counts in icterus neonatorum.

4. The total leukocyte count at birth averages 16,600 per cubic millimeter. At twelve hours it is 22,500, after which it gradually drops to 11,300 at forty-eight hours. At five days it has decreased to 9,500.

5. The differential counts show wide variations. The averages present curves which are often quite different from those reported in the literature. One of the striking features observed was the marked changes which may take place within a very few hours. In one instance the white count jumped from 25,000 to 34,000, while the P. M. N.'s

increased from 38 to 61 per cent. within six hours. It is important in any differential blood study to determine the absolute cell counts as well as the percentages. The curves often differ from each other to a great extent.

6. The P. M. N. neutrophils follow closely the total white count, and are primarily responsible for the leukocyte curve in the new-born period.

7. The neutrophilic metamyelocytes are very numerous in new-born blood. Values as high as 43 per cent. have been observed in this study. Our findings agree closely with those of Arneth on nuclear lobes in the neutrophils. Neutrophilic myelocytes are infrequent in new-born blood; they are most numerous during the first eighteen hours.

8. The absolute values of the lymphocytes vary little during the first five days. At birth and six hours after they are most numerous. There is a slight drop at twelve hours followed by a fairly constant number until forty-eight hours after birth. Between forty-eight hours and five days there is a moderate increase. The percentages show a definite increase in values from twelve hours to five days. The curves taken by the small, medium and larger lymphocytes are quite similar to the curve of the total lymphocytes.

9. The leukocytoid mesolymphocyte is not so commonly seen as is the large lymphocyte. The small lymphocytes are more numerous than the large. Whenever an absolute lymphocytosis occurs, the relative number of small and large lymphocytes is increased at the expense of the medium sized ones. Early forms of lymphocytes are quite common in the first twelve hours of life.

10. The relative and absolute values of lymphocytes and neutrophils are equal at forty-eight hours. After this time the values for the lymphocytes increase while those of the neutrophils decrease.

11. The mononuclears and transitionals are present in the same percentages as later in life. Both are more numerous during the first few hours.

12. The eosinophils gradually rise in number until thirty hours after birth and then become less numerous. The percentage curve shows an increase up to forty-eight hours. Eosinophilic metamyelocytes are occasionally seen. They are commonest at from thirty to thirty-six hours when the adult eosinophils are most numerous. They never form more than 0.4 per cent. of the cells.

13. Basophils are rare in new-born blood; they are most numerous at birth.

14. The Rieder cell is most frequently seen during the first twenty-four hours.

15. The plasma cell is rarely seen until five days after birth when it occasionally is present.

16. The "unusual" cell, or atypical neutrophilic promyelocyte, occurs occasionally during the first twenty-four hours, but rarely thereafter.

17. The frequency of degeneration forms of leukocytes in general varies directly with the total white count. They have been divided into three groups. The lymphocyte and neutrophil forms closely follow the curves of their respective types. In the case of the eosinophils, degeneration increases between forty-eight hours and five days, despite the fact that the eosinophil count diminishes during this period. The degeneration is probably due to an increased vulnerability of the leukocytes as a result of their overproduction during the first few days of life.

18. The nucleated red blood cells have been divided into four groups. In two groups the nuclei have a definite structure. The cytoplasm in one is acidophilic, in the other polychromatophilic. In this series of cases polychromatophilic nucleated red cells were much more commonly seen than those with acidophilic cytoplasm. The latter appeared only when there was marked increase in erythroblast formation, at which time microblasts, megaloblasts and even mitotic figures were seen. Naked red cell nuclei without cytoplasm were frequently seen when many nucleated red cells were present.

Every case studied showed nucleated red blood cells. At forty-eight hours about 50 per cent. had them, while at five days only one case showed one normoblast.

19. Normal new-born blood shows a lesser tendency to rouleaux formation than does normal adult blood. Basophilic stippling was not observed in this study. Anisocytosis and polychromatophilia are always present in the blood of the new-born. Poikilocytosis is often present. The pear shaped cells are usually smaller and paler than the poikilocytes seen in severe anemias.

20. The platelets are often larger in the new-born blood than in that of the normal adult. Their variations in size are greater than those ordinarily seen in the adult.

21. The neutrophil and eosinophil granulation is similar to that seen in adult blood. The azure granules tend to be less numerous, but when present, their size, distribution, and staining reaction are the same as in the average blood smear of a normal adult.

22. In five cases of marked icterus neonatorum no changes from the normal were noted in the total cell counts or in the differential counts.

23. The standard deviation and the coefficient of variability were determined for the absolute and relative counts of all types of blood corpuscles. The findings may be summarized as follows: (*a*) The red

blood cell count was the least variable of any of the cell counts, and its coefficient of variability averaged about 11 per cent. It stands midway between the variability in height and the variability in weight of the child at birth; (*b*) the variability of the blood platelets is very great at all times and averages over four times that of the red blood cells; (*c*) the coefficient of variability of the leukocytes is about from 20 to 25 per cent., or about one-half that of the platelets and twice that of the red blood cells; (*d*) the coefficient of variability of the total polymorphonuclear leukocyte count averages about 35 per cent., being about one half more than that of the total leukocyte count; (*e*) the coefficient of variability of the total lymphocyte count is about the same as that of the polymorphonuclear. It tends to decrease during the period of observation; (*f*) the variability of the cells having lesser total counts is very great, the coefficient of variability ranging from 85 to 200 per cent. In most instances the variability becomes less after the first day; (*g*) the nucleated red corpuscles are also very variable. The coefficient of variability reaches its maximum at about 215 per cent. on the second day; (*h*) the percentage counts of the various types of cells are, as a rule, more constant than the absolute counts; (*i*) the percentages of the commoner varieties of circulating blood cells, the lymphocytes and the polymorphonuclear leukocytes, show a coefficient of variability of from 20 to 25 per cent. The remaining varieties have a coefficient of variability of from 50 to 80 per cent., except for the basophils which have a variability of 100 to over 200 per cent.

24. The changes observed in the red blood cell, platelet and leukocyte count cannot be accounted for on the basis of blood concentration. The differential study emphasizes the fact that the variations noted in the new-born period are due to increased activity of the hemopoietic organs.

The evidences for increased neutrophil production are: (*a*) The polymorphonuclear leukocytosis, (*b*) the large numbers of metamyelocytes, (*c*) the presence of neutrophilic myelocytes, (*d*) the occurrence of unclassified promyelocyte types, (*e*) the increased vulnerability of neutrophils, (*f*) the very small P. M. N. neutrophils, (*g*) the occurrence of cells in which the cytoplasm is basophilic and the nucleus polymorphous.

The facts indicative of increased lymphocyte production are: (*a*) Early types of lymphocytes, (*b*) the presence of cells undergoing amitotic division, (*c*) the presence of Rieder cells, (*d*) the presence of plasma cells, (*e*) atypically large lymphocytes, (*f*) the increased vulnerability of the lymphocytes. (*g*) the occurrence of occasional Türke's irritation cells. Evidences in support of the concept of increased red cell production are: (*a*) polychromatophilia, (*b*) anisocytosis is always present, (*c*) poikilocytosis is occasionally seen, (*d*) nucleated

reds are found in every new-born infant's blood, (*e*) megaloblasts are frequently observed, (*f*) naked red cell nuclei are often seen, (*g*) mitotic figures are present in instances of markedly increased numbers of nucleated red blood cells.

I wish to acknowledge my indebtedness to Dr. Scammon, under whose direct supervision this work was done. Without his valuable suggestions in all the phases of the problem, especially in the section on statistics, this study could not have been accomplished. I also wish to thank Dr. Hal Downey for his kind assistance in the hematologic section, and Miss Pearl Shalit for her services.

Abstracts from Current Literature

Anatomy and Physiology

THE VALUE OF THE HEMOGRAM IN INFANCY. CURT and STECHER FRANKENSTEIN, Ztschr. f. Kinderh. **37**:145, 1924.

The hemogram, or differential cell count of premature infants, shows the definite shifting to the left of Arneth. Many immature polymorphonuclear leukocytes are found there. The hemogram of full term new-born infants is also easily distinguished from that of adults. This differential cell count is of great value in the diagnosis and prognosis of disease in infants, especially in the acute infections, atrophy, and intestinal disturbances.

PETERMAN, Rochester, Minn.

INNERVATION OF THE VENO-CONSTRICTOR MECHANISM OF THE LIVER. HANS MAUTNER, Monatschr. f. Kinderh. **27**:385, 1924.

The conclusions are based on the following technic. A clamp was placed on the pulmonary artery causing a back-flow of blood into the liver, and then different drugs were investigated as to whether their effect increased or decreased the size of the liver's swelling.

In this way, Mautner concludes that the influence of the vagus, as well as split protein products, peptone, histamin and water tend to cause constriction. On the other hand, stimulation of the sympathetic, as well as diuretics and hypertonic solutions, cause dilation.

GERSTLEY, Chicago.

Pathology, Bacteriology and Biochemistry

A BIOLOGIC STUDY OF ACIDURIC BACTERIA. PAUL R. CANNON (University of Mississippi), J. Infect. Dis. **34**:227 (March) 1922.

A biologic study of sixty-four strains of *B. acidophilus* and thirty-four of *B. acidophil-aërogenes* was made. These organisms were isolated from ninety-three different sources, mostly from the sputum and feces of normal human adults. Dried autolyzed yeast was used as the basis for all the fermentation tests, and was particularly satisfactory for the study of these members of the aciduric group.

These bacteria are facultative anaërobes, but will grow well under aërobic conditions. They do not liquefy gelatin, and may or may not clot milk. They grow best in a reaction of p_H from 6 to 7, but will develop within the range of p_H 5.0 to 7.6 at least. When grown in dextrose yeast broth in mixed culture with *B. coli*, with an initial reaction of p_H 7.0 to 7.6, *B. coli* at first gains the ascendency, but *B. acidophilus* becomes predominant as the p_H approaches 5.

In the case of twenty-two strains, both aciduric and fermentative characteristics were practically constant for twelve months. The fermentation reactions for twenty carbohydrates were determined, all negative tests being checked at least twice.

A classification according to the scheme of Rahe is given.

KENNEDY, Rochester, Minn.

CLINICAL AND EXPERIMENTAL EVIDENCE OF THE VIABILITY OF TRANSFUSED FOREIGN ERYTHROCYTES. HANS OPITZ, Monatschr. f. Kinderh. **27**:376, 1924.

The question to be answered was whether the benefits derived from blood transfusions were due to the foreign red cells themselves, or to the stimulus of the foreign blood on the child's bloodmaking organs. To solve this,

Opitz injected separately both plasma and washed erythrocytes into an anemic child. He also injected whole blood and hemolyzed blood into a number of animals. By blood counts and blood chemistry he came to the conclusion that the good results are from the injected red cells themselves and that these remain viable for considerable time.

GERSTLEY, Chicago.

THE RELATION OF THE SUBSTANCE RESISTING SAPONIFICATION TO RICKETS. H. BEUMER, Ztschr. f. Kinderh. **37**:105, 1924.

Experimental evidence is cited, in support of the theory that the antirachitic substance in cod liver oil is found in that portion which cannot be saponified.

PETERMAN, Rochester, Minn.

Nutritional Disturbances

DO HEIGHT AND WEIGHT TABLES IDENTIFY UNDERNOURISHED CHILDREN? LOUIS I. DUBLIN and JOHN C. GEBHART. Statement by LOUIS C. SCHROEDER. New York Association for Improving Conditions of the Poor, New York, 1924.

This timely article brings out an important principle: namely, that the determination of normality in children does not rest on any set weight standards. The investigation was made among the Italians of New York City and consisted of examination and records of 1,878 boys and 2,169 girls. It was found by this examination that 77.2 per cent. of the boys and 67.1 per cent. of the girls who were actually undernourished would have been missed entirely if reliance had been placed solely on the standard of the 7 per cent. under weight. With the 10 per cent. standard 89.8 per cent. of the boys and 81.8 per cent. of the undernourished girls would have been lost. On the other hand, in the well nourished children 97.6 per cent. boys and 94.5 per cent. girls were found to agree with the standard weight tables.

The main part of the article is supplemented by a short statement by Dr. Schroeder, regarding the standards he used in choosing these children and in designating them as undernourished. This article only lays further emphasis on the fact, well known to the medical profession, that final decision regarding nutrition normality in children depends not on single standards such as weight but on complete physical examination which can only be conducted by a properly equipped physician.

GRULEE, Chicago.

THE INFLUENCE OF ENVIRONMENT ON THE NUTRITION OF GROWING ANIMALS. RUDOLF DEGKWITZ and fifteen assistants, Ztschr. f. Kinderh. **37**:27, 1924.

In an effort to determine the influence of light on cell metabolism of young, growing animals, Degkwitz and his assistants carried on a large series of feeding experiments on young dogs. Pairs of dogs were selected from the same litter; one dog of each pair was kept in natural light, the other in darkness. Various diets were fed:

Light

Protein		*Carbohydrate*	
Low value fat (Light dog).....	L_1	Low value fat.....	L_3
Full value fat.....	L_2	High value fat.....	L_4

Dark

Protein		*Carbohydrate*	
Low value fat (Dark dog).....	D_1	Low value fat.....	D_3
Full value fat.....	D_2	Full value fat.....	D_4

After five months the animals were killed and examined: Anatomic, pathologic, and chemical examinations were made. The two animals of each pair were compared and the various organs analyzed. High value fat, when

fed in combination with a large amount of protein exerted the most favorable influence on the skeletal growth. Low value fats, such as cocoa butter, plus an excess amount of carbohydrates caused the least growth. Light absence produced a lowering of the metabolic rate and changes in the chemistry of the ash residue similar to those found in rachitis.

In the interpretation of the findings, the author considers the possibility of adaptation of the animals to darkness. He also mentions a number of important factors which must be considered in an interpretation of experiments of this kind. Apparent well-being and gain in weight are not reliable criteria of nutrition results. The entire body must be examined and the ash residue analyzed to make complete conclusions.

Pairs of healthy young dogs as nearly alike as possible were selected. Following the experiment, the dogs were clinically and pathologically (sections, histology) well. Every dog kept in darkness showed a greater increase in weight than his control. The amount of the total body weight increase was influenced by the quality of fat. The soft tissue growth was equally good whether high value fat was fed with high protein or high carbohydrate. Since a sufficient amount of vitamin was supplied, the variations in growth can be ascribed to the fat. In the dogs kept in darkness the ash residue showed a relative decrease in calcium, phosphorus, sodium and magnesium, while the potassium showed a relative or absolute increase. The absence of light did not cause rachitis but caused a predisposition to rachitis. The soft tissues and the bones showed a calcium and phosphorus decrease. Histologically, the bones could not be distinguished.

PETERMAN, Rochester, Minn.

THE INFLUENCE OF HIGH PROTEIN CONCENTRATION IN INFANT FEEDING. MARIANNE ECKERT, Ztschr. f. Kinderh. **37**:1, 1924.

Eight healthy infants, from 5 days to 6¾ months of age, were placed on a concentrated albumin feeding. The infants were fed Dubo (whole milk with 17 per cent. sugar) with an increased albumin content of from 30 to 40 per cent. The increase was held at 30 per cent. for twenty-four to sixty hours and then increased to 40 per cent. In one case the 40 per cent. increase was maintained for six days. Following the high protein diets there was noted, regularly, a loss of weight without symptoms of ill health. The food was well taken. The stool was often foul smelling and somewhat mucoid. Following this diet there was no increase in the cellular elements of the blood and there was no increase in the serum protein. There was no elevation of temperature in any case. Return to the former diet was followed by an increase in weight without temperature changes. Eckert (and Pirquet) cannot subscribe to the "dynamic protein fever" theory, if water is given freely. At least there was no increase in the temperature following a concentrated protein diet in the eight cases studied. However, only two protein preparations were used (albulactin and aleuronat). Protein concentrations higher than 20 per cent. are not well tolerated.

PETERMAN, Rochester, Minn.

THE PATHOLOGY OF MILK INJURY, PART 2. FEEDING, STOOL, CHARACTERISTICS AND BIFIDUS-FLORA. REINHOLD RUHLE, Jahrb. f. Kinderh. **104**:39 (Jan.) 1924.

The pathogenesis of "milchnährschaden" is connected in some way with bacteriochemical processes in the large intestine and is related to the kind of food. The author's purpose is to determine the degree of dependence of the bifidus flora on different components of breast milk, and if possible to produce a physiologic bifidus flora by dietary changes on artificial feeding. He studied 3,000 stools of normal infants from 2 to 7 months of age, as regards consistency, color, reaction to litmus, odor, and gram-stains of stool for flora.

He found that replacement of fat in artificial feeding by breast milk fat and in breast feeding by butter fat, did not change the characteristics or flora of

the stools. Addition of cereals to breast milk up to 3 or 4 per cent. had no influence on the stools; addition of calcium salts and sodium phosphate up to 1.5 per cent. gave more alkaline and brighter colored, firmer and less frequent stools with degenerative bifidus forms, and more *B. coli* and cocci. The addition of egg albumen did not affect stools, though cow's serum to 5 per cent. changed stools toward those of "milchnährschaden." *B. coli* predominated. Removal of casein and whey protein did not give a bifidus flora.

By one method, he was able to produce bifidus flora and stool characteristics on artificial feeding in some, though not in every case; i. e., by using the filtrate of skimmed milk predigested, with pepsin plus an equal amount of water and 5 per cent. lactose plus 6 per cent. butter plus 3 per cent. "Weizenmehl" (wheat flour). None of the known artificial foods have produced this result.

In this paper, the author is dealing only with normal infants, so no therapeutic results of this mixture are presented.

SUTHERLAND, Chicago.

EXPERIMENTS CONCERNING THE BACTERIAL INVASION OF THE INTESTINAL TRACT, AND ITS INFLUENCE UPON FOOD. EUGENE STRANSKY, Monatschr. f. Kinderh. **27**:388, 1924.

Professor Moll has shown that rabbits fed on a onesided milk diet become hyperirritable to electricity and show signs of nutritional disturbance. Stransky kept a number of animals on this diet until he had affected their state of nutrition and then made smears and cultures from the mucosa of the stomach and various parts of the intestine. The sick rabbits showed *B. coli* in smear and culture, besides a variety of other organisms throughout all parts of the gastro-intestinal tract.

The control rabbits showed isolated colonies in the stomach and duodenum. The small intestine, as far as the lower ileum, was sterile, after which *B. coli* were found in large numbers.

The experiments repeated on dogs did not give identical results. At no time was any part of the intestine of these animals found sterile.

The experiments were repeated on rats. The findings were intermediate between those of the dog and of the rabbit, being more frequently, however, like the rabbit. Of interest was the observation that if vitamin was absent from the diet, bacterial growth was luxuriant throughout the whole intestinal tract.

GERSTLEY, Chicago.

Prenatal Conditions

THE VALUE OF THE ROENTGEN RAY IN THE DIAGNOSIS OF ATYPICAL PREGNANCIES, WITH REPORT OF TWO CASES OF ANENCEPHALY DIAGNOSED BEFORE BIRTH. DAVIS SPANGLER, Am. J. Roentgenol. **11**:238 (March) 1924.

Aside from the diagnosis of pregnancy and its position the roentgenogram is of value in determining the degree of contracted pelves, spinal curvature, the diagnosis of multiple pregnancy and as a medicolegal factor. The author feels that a roentgenogram should be taken before a cesarean section operation is undertaken, and except in extreme emergency, before operative interference in eclampsia. This obviates the embarrassment of delivery by cesarean section of a monster, a dead fetus or an extremely small baby. The size can be fairly well determined and the modus operandi may be arrived at in doing version on a foot or transverse presentation.

Anencephaly, or craniorrhachischisis, is one of the most frequent of fetal monstrosities. Kirkness, in 1911, reported one in every 900 deliveries in a series of 11,521. Of the theories involved, the author mentions early hydrocephalus with secondary rupture and atrophy of cranial membranes, changes or toxins in the amniotic fluid and faulty implantation of the ovum due to changes in the endometrium. In the two cases reported the anencephaly was diagnosed by roentgen ray, which showed the lack of cranial bones, and the

diagnosis was confirmed by the pathologist after delivery. The author regards the idea that the roentgen ray may be harmful to the fetus as fallacious.

STULIK, Chicago.

Acute Infections

BRONCHOPNEUMONIE DU NOURRISSON. JEAN MEYER, Thésè de Paris, 1923.

The first part of this thesis is taken up with a clinical résumé of the condition. The author then speaks of two specific conditions—the asphyxial and the septic-toxemic states—which he describes in detail. The former, as may be supposed, tends to cyanosis and is accompanied by rapid breathing; the temperature is variable but is usually quite high. The septic-toxemic state is characterized by diminution in weight, suppression of urine, the usual facies, loss of appetite and diarrhea. The child refuses the bottle, thirst seems to have disappeared, the skin is flaccid, subcutaneous injections of fluids are only slowly absorbed, the heart is very rapid and the liver is enlarged and hard. This period does not last more than two or three hours. Just before death the body is covered with sweat, the pulse becomes very weak, and respiration is slow.

The author has then undertaken to study first, the asphyxial state, and later the septic-toxemic. Asphyxia or "anoxemie" depends on the retention of oxygen in the arterial blood. The lowering of this tension is the essential factor, and is characterized clinically by cyanosis, and an excessive lowering means the irremediable failure of the vital processes. As to the cause of this condition one may, of course, regard it as due to the diffuse pulmonary lesion but it also may be due to a failure of the tissue tolerance for oxygen. In other words, the tissues may be unable to take up the oxygen because of the toxic condition.

In the toxic infections he has taken into consideration two syndromes, the anorexia and the variation of the weight curve. The weight curve is due to the water content of the body increased with edema and decreased with dehydration. Special study has been made of the condition of perspiration. This study was made in the following way: The basal perspiration was that of a child awake and calm, proportion of twenty-four hours. Due account was taken of the amount of urine, stool and carbon dioxid excreted. A calculation was made from the food and the excreta, the difference being regarded as the basal perspiration. Hourly weights were then taken. In the normal child the relation of basal perspiration to elimination daily was about from 40 to 50 per cent., while in bronchopneumonia it was about 80 per cent. This runs parallel to the dehydration. In some, however, the perspiration was abnormally low caused by retention of the water.

He also examined the caloric loss in infants and found in the normal cases it amounted to from 60 to 70 per cent. In bronchopneumonia it is sometimes increased and sometimes diminished, but the intake of the food is always reduced and the relative size of the caloric loss is considerably increased. In normal infants half of the heat eliminated is by perspiration and the other half by radiation. In bronchopneumonia perspiration eliminates about 90 per cent. and the rôle of radiation is diminished.

One of the chief factors, therefore, in equilibration of tissue exchanges, caloric equilibrium and thermal regulation is perspiration.

The last of the treatise is taken up with a short chapter on prognosis, which contains nothing new, and on treatment. He strongly advises fresh air and sunlight, to prevent the child from chilling, and also change of position to prevent hypostatic pneumonia. The diet should be as abundant as possible. Warm baths are advised. He advises also serotherapy, not for its specific but for its general tonic effect. This necessitates large doses. For asphyxial syndrome oxygen is of value. Stimulation is likewise mentioned.

GRULEE, Chicago.

BONE DYSTROPHIES OF VARIOLA. J. W. CATHCART, Am. J. Roentgenol. **11**:229 (March) 1924.

The author cites the work of Chiari, who reported nonsuppurative, sterile necrotic foci in the bone marrow in twenty-two necropsies on variola cases of different stages. Mallory found these foci in fourteen patients dying of variola and notes that they were more numerous in the short bones. Patients of the first age period who have variola may have these necrotic areas so situated as to involve the ossific centers and so alter the future development of the bone. The epiphyses may become altered and ankylosis, fusion and exostosis are frequently resultant. As a rule the greater deformity is found where the variola infection occurs in the first years of life.

Musgrave and Sisson reported deformities of the forearms and hands caused by variola contracted early in life. All of their twenty cases were native Filipinos.

A girl, American, aged 6 years, living in Mexico contracted severe variola three years ago, and during three months in bed the severe pains in the arms and legs simulated rheumatism. She gradually developed deformities of the forearms and wrists. The roentgenogram shows that the left ulna extended 2 cm. beyond the radius and deflected the hand to the radial side. There was a suggestive old necrosis of the lower end of diaphysis, and in the thickened radius the distal epiphyseal line was obliterated. In the right forearm the radial epiphysis of the elbow and the distal epiphysis of both ulna and radius were obliterated and the radial shaft was bowed out. There were old necrotic areas in the tibia and fibula of the left leg. The right clavicle was 2 cm. shorter than the left.

In the discussion, Phemister, before seeing the work of Musgrave, was inclined to consider the condition one of osteomyelitis of the metaphyseal regions due to pyogenic organisms entering through the skin.

STULIK, Chicago.

SPECIFIC STREPTOCOCCUS AGGLUTININS IN CONCENTRATED SCARLATINAL SERUM. R. D. HERROLD and RUTH TUNNICLIFF, J. Infect. Dis. **34**:209 (March) 1924.

Concentration with ammonium sulphate is useful for demonstrating specific streptococcus agglutinins in scarlatinal serum. Unconcentrated scarlet fever serum 1:10 fails to agglutinate hemolytic streptococci, specific for sarlet fever. When concentrated with ammonium sulphate, 25 per cent. of the scarlet fever serums collected before the eleventh day of the disease, and 92 per cent. of the serums collected after the eighteenth day, agglutinated scarlatinal strains of streptococci, but not the other streptococci tested. Serum, unconcentrated, and concentrated from diphtheria patients and from a patient who had scarlet fever two years previously, failed to agglutinate any of the streptococci examined.

KENNEDY, Rochester, Minn.

THE INFLUENCE OF SCARLATINA AND DIPHTHERIA ON THE HEART. A. F. HECHT, Ztschr. f. Kinderh. **37**:5, 1924.

Nine cases of cardiopathy which had developed during diphtheria were examined sixteen years after the onset of the infection. Seven per cent. of the patients had residual cardiac lesions, for the most part myocardial weakness. Six cases had developed cardiac complications during scarlatina nine and a half to twelve and a half years previously. Two patients had residual mitral lesions. The cardiac complications which develop during scarlatina offer a much better prognosis than those developing in diphtheria.

PETERMAN, Rochester, Minn.

AGGLUTININS FOR PFEIFFER BACILLUS IN SERUM OF INFLUENZA AND MEASLES PATIENTS. W. B. SHARP and E. O. JORDAN, J. Infect. Dis. **34**:305 (March) 1924.

Sharp and Jordan studied the serums of twenty-nine influenza patients, twenty-nine measles patients and twenty-seven other persons in regard to their power to agglutinate the Pfeiffer bacillus. They found that the serum of influenza patients agglutinates Pfeiffer bacilli to a greater degree and in a larger number of cases than does the serum of healthy persons.

Serum of measles patients does likewise, so that the presence of agglutinins for the Pfeiffer bacilli in influenza serum cannot be taken as evidence of any causal relation between the organism and influenza. There is no evidence that the observed increase in agglutinative power in measles serum is dependent in any degree on a secondary invasion by the Pfeiffer bacilli. The most plausible explanation seems to be that infections of various kinds increase the nonspecific or normal agglutinins of the blood, and that such relatively slight agglutination enhancement as is observed falls in this category and not in that of specific causal relation.

KENNEDY, Rochester, Minn.

USE OF THE ROENTGEN RAY IN PERTUSSIS. R. D. LEONARD, Am. J. Roentgenol. **11**:264 (March) 1924.

In collaboration with the staff of the Floating Hospital, 450 cases of clinical pertussis were examined and treated. The entire chest and lower neck alternating front and back were treated with a 5 ma. dose with a 6 inch spark back-up for four minutes, at a focus skin distance of 14 inches using a 1 mm. aluminum filter. This small dosage was used to prevent harm to the skin, thyroid or thymus.

Under the direction of Mallory not a single positive culture of the Bordet bacillus was obtained from nose, pharynx, larynx, trachea or turbinate curetting. In the one fatal case Mallory demonstrated the Bordet bacillus within the tissue of the trachea. This may be due to the fact that most of the cases were seen at the height of the paroxysmal stage and not at the early catarrhal stage.

Each child was given four treatments, unless marked improvement followed the second or third treatment. The treatments were given two days apart.

The bronchial glandular enlargement observed was much greater than that noticed in chests of children with measles, scarlet fever or diphtheria. It is the author's theory that the direct action of the roentgen ray on the bronchial lymph nodes produces the relief of symptoms.

There was a diminution in the severity of the paroxysms, and frequently a marked diminution in the number and vomiting was promptly relieved.

Compared to 200 cases untreated with roentgen-ray therapy, the course of the disease was definitely shorter only in the children from 1 to 2 years of age in the treated group. Exact comparison cannot be made, because many of the children treated with roentgen ray were also getting medication including vaccine.

In the discussion, Dr. Dunham regards the benefit due to aid in resolution of the simultaneous pneumonic condition, and Dr. Leonard states that there is some general effect besides local effect on the glands. The problem is to arrange for these children in a separate institution or in a roentgen-ray whooping cough clinic.

STULIK, Chicago.

Chronic Infections

THE INFLUENCE OF PERTUSSIS ON TUBERCULOSIS. ERNST and FUERST KOENIGSBERGER, Ztschr. f. Kinderh. **37**:159, 1924.

In thirteen tuberculous children under 2 years of age, who developed pertussis, tuberculosis became active in nine. Sixty-one tuberculous children, from 2 to 14 years of age, developed pertussis; in six the tuberculosis became

active. Of two hundred forty-six children with tuberculosis only fourteen cases had been preceded by measles, and four by pertussis. The tendency to exacerbation of a tuberculosis is much greater following measles than it is following pertussis.

PETERMAN, Rochester, Minn.

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGICAL POINT OF VIEW. No. X, ARSENIC IN HUMAN MILK AFTER INTRAVENOUS INJECTION OF SALVARSAN. J. A. FORDYCE, ISADORE ROSEN and C. N. MYERS, Am. J. Syphilis **8**:65 (Jan.) 1924.

Arsenic was not present in any considerable quantity in the milk of fifteen control cases under hospital conditions. Seventy-five specimens of milk from twelve mothers receiving active antisyphilitic treatment, were examined. After 0.6 gm. neo-arsphenamin, the average excretion in the milk expressed in milligrams of metallic arsenic per one hundred grams of dried specimen was: The first day, 1.25; second, 1.16; third, 0.70; fourth, 0.98; fifth, 1.31. The arsenic excreted in five days would be equivalent to about 0.03 gm. of neo-arsphenamin. The presence of arsenic in mother's milk is more constant than in either the blood or urine, and was found in appreciable amounts in one case four months after the last arsphenamin injection. A nursling, therefore, receives sufficient arsenic in the breast milk to be of "some therapeutic value." There should be energetic treatment of the mother during lactation, in addition to other forms of treatment of the infant.

SUTHERLAND, Chicago.

Internal Diseases

ACUTE ALEUCOCYTEMIC LEUKEMIA IN CHILDHOOD. H. BAER, Jahrb. f. Kinderh. **104**:1, 1924.

This is a detailed description and discussion of three fatal cases from 7 months to 7 years of age, having a hemoglobin of from 14 to 22 per cent., a color index of 1 + and a white count of 2,000 to 6,000. The symptoms covered a period of from one to two months before admission. There was extreme weakness, pallor and loss of appetite, slight fever and a tendency to hemorrhages especially into the gums. The spleen and liver were enlarged. These cases were considered leukemic on account of the predominance in the blood smears of lymphocytes and lymphocyte-like cells, (87 per cent.) and the small number of polymorphonuclear leukocytes (8.5 per cent.). There was also a diffuse lymphocytic infiltration of the lymph glands and the interlobar connection tissue of the liver. Two of these cases were of the myeloid type, and one a mixed myeloid and lymphatic. The etiology is unknown.

The blood picture of these acute leukemias is similar in several respects to that of aplastic anemia, but the course is more acute and the bone marrow is richer in cells with more nucleated red cells. The author considers acute leukemia to be much more common than aplastic anemia in children.

SUTHERLAND, Chicago.

ADRENAL. ERWIN THOMAS, Monatschr. f. Kinderh. **27**:343, 1924.

Thomas brings the literature of the adrenal up to date. The main evidence of the function of the gland as exhibited by cases of hypertrophy, is that it seems to be a factor leading toward masculinization, women with such tumors seeming to take on somewhat masculine qualities.

The gland seems perhaps to be part of a protective mechanism against poisons, as hemorrhages in the medulla are found in some cases of poisoning, and marked changes in the gland in fatal cases of scarlet fever and streptococcus septicemia.

The gland in its composition contains neutral fat and fatty acids, cholesterin and its esters and lipoids. Of these, the cholesterin especially, is stored,

particularly in herbivora. It is questionable whether this process occurs in carnivora.

Of course the secretion of the medulla, the blood pressure raising element known as adrenalin, has long been described. Besides this, the gland may possibly have some concern with the metabolism of vitamins.

As regards its diseases, Addison's disease is very rare in children. Hemorrhage into the gland is not so very uncommon and is fatal in twenty-four hours.

Of interest is the observation that the adrenal is especially large in the new-born.

GERSTLEY, Chicago.

THYMUS GLAND. W. BIRK, Monatschr. f. Kinderh. **27**:321, 1924.

The usual methods of studying glandular function are rather difficult in the case of the thymus. Congenital absence is extremely rare without changes in other organs which might confuse the picture of pure absence of the thymus. Hypoplasia of the thymus might readily be confounded with normal involution. Furthermore, results of surgical removal are most uncertain. The conclusions of observers are utterly conflicting, and the findings ascribed by some investigators to removal of the thymus were probably due to poor hygiene of the kennels in which the animals were kept.

Studies by implanting grafts of thymus are more satisfactory than those concerning themselves with its absence. In certain animals, implanting thymus into the muscles leads to increased growth of that animal.

When all is said and done, our knowledge of thymus is based to a considerable extent on clinical observation. The association of sudden death with enlarged thymus has long been noted. Paltauf was one of the first to emphasize this association, but thought it was merely a coincidental finding, the main factor being a cardiac weakness. Escherich somewhat amplified this view by laying increased significance to the so-called "thymic constitution," believing the depression of the heart to be caused by an excessive thymic secretion.

These ideas have been challenged by a number of observations. Some cases of sudden death have been traced to myocarditis from other causes. Some cases have been found associated with hypoplasia of the chromaffin apparatus. Richter's idea is well known; namely, that the thymus is found to be large in practically all cases of sudden death, but that this is a normal finding, for, in cases of disease, the thymus atrophies so quickly that on necropsy it is found to be abnormally small. Lastly, the idea of hypersecretion has been attacked by the observation that the sudden death has been due to suffocation caused by the pressure of the enlarged organ.

Birk still believes, however, that a very small group of cases of sudden death may be explained on a hypersecretion basis. His reasoning is clinical. First, a certain number of patients with Basedow's disease die suddenly on the operating table. Necropsy reveals an enlarged thymus. Hence the reasoning that excessive thymic secretion might be a cause. Another argument of Birk's is the lymphocytosis found in status lymphaticus is found in other conditions associated with thymus hyperplasia, such as myasthenia gravis. This might suggest an excessive thymus secretion.

Birk concludes his article by attempting to show that the thymus is related to the testis, ovary, adrenal, thyroid and parathyroid.

GERSTLEY, Chicago.

THYROID GLAND. E. SCHIFF, Monatschr. F. Kinderh. **27**:359, 1924.

It is interesting to note that aplasia of the thyroid gives no symptoms for some weeks after birth. In all probability the child is born with a supply. Schiff makes the statement that the fetal thyroid contains no iodin, but in the discussion following his paper this point was disputed.

As regards the functions of the thyroid, besides its effects on metabolism, it is undoubtedly concerned to some extent in the mechanism of growth, for all cretins are dwarfs.

In myxedema there is a popular tradition that the tolerance of the body for sugar is effected. This is not invariably true. There are perhaps vagotonic and sympathicotonic types of this disease which have their effects on sugar tolerance and muscle spasticity.

The child has a remarkable tolerance to thyroid and even through the school age, goodly doses of the extract while causing the same objective symptoms as the adult, do not seem to cause the child the same subjective sensations.

As regards the diseases, a true form of Basedow's disease is very rare in a child. The question of cretinism is not settled either. It is definitely related to the thyroid, but just how is uncertain.

In treatment, thyroid extract is of value in myxedema, but is not a cure. It seems to bring the patient to a certain stage and beyond that it does no further good.

GERSTLEY, Chicago.

CALORIMETRIC STUDIES ON INFANT CRETINS. FRITZ TALBOT, Ztschr. f. Kinderh. **37**:98, 1924.

The technic of the Talbot basal metabolism determination of infants is described in detail. The readings in two cases are given and the results of treatment enumerated in tables. Hypothyroidism presents a definite low basal metabolic rate during the first six months of life. These cases, according to Talbot, can be diagnosed only by obtaining the basal metabolic rate.

PETERMAN, Rochester, Minn.

THE CONSTITUTION AND REACTIONS OF THE NERVOUS CHILD. CARL POTOTZKY, Ztschr. f. Kinderh. **37**:24, 1924.

Zappert's classification of the neuroses of childhood, although more elaborate, suffers from the same defects as the more simple classification. Zappert divides the neuroses into: 1. Neuropathies. 2. Psychopathies. 3. Habit Neuroses. 4. Imitation neurosis. 5. Anxiety neuroses. 6. Compulsion neuroses. 7. Hysteria.

Pototzky's classification consists of: 1. Neuropathies. 2. Psychopathies. 3. Hysteria. Both classifications, he says, group together many unequal and dissimilar factors.

PETERMAN, Rochester, Minn.

THE PATHOGENESIS AND THERAPY OF TETANY. KURT SCHEER and ADOLF SALOMON, Jahrb. f. Kinderh. **104**:65 (Jan.) 1924.

The authors present further work on the mineral metabolism in spasmophilia as affected by hydrochloric acid milk, calcium chlorid and ammonium chlorid. Scheer had previously demonstrated that hydrochloric acid milk decreased the electrical and mechanical excitability. In this series, the calcium content of the blood serum, which is decreased in spasmophilia, was definitely increased toward normal under treatment with hydrochloric acid milk and by calcium chlorid.

The acid soluble phosphate was increased in tetany; the lipoid phosphorus varied being slightly increased in usual tetany cases, but distinctly decreased in the severe cases.

The calcium phosphorus quotient was decreased and this in inverse ratio to $\frac{\text{acid soluble phosphorus}}{\text{lipoid phosphorus}}$. With treatment, there was generally a rapid drop in acid soluble phosphorus, and in high phosphate tetany, an increase in lipoid phosphorus. The changes in calcium content were slower.

SUTHERLAND, Chicago.

Surgery and Orthopedics

THE SURGICAL TREATMENT OF LATERAL CERVICAL FISTULAE. FREDERICK CHRISTOPHER, Surg. Gynec. & Obst. **38**:329 (March) 1924.

The work of Wenglowski in 1912 brought out the fallacy of the branchiogenetic theory of the origin of lateral cervical fistulas. His ideas are based on a study of serial sections of seventy-eight embryos, 147 child cadavers and fifty-nine adult cadavers, besides a study of twenty-one cases of actual neck fistulas or cysts. His conclusions are as follows:

1. In man five or six branchial arches develop, and the same number of clefts or grooves. The grooves are not open.

2. The neck sinus—sinus cervicalis—is built by the approximation of the lateral borders of the neck, breast, and under border of the third arch and not the second as His contended.

3. In embryos as well as in adults the branchial apparatus does not lie from above downward but from front to back. Its inferior border and the inferior border of that part which arises from it are made by the line which passes through the inferior border of the hyoid bone.

4. In the beginning of the second month, the entire branchial apparatus as such disappears. It may leave behind it portions of many layered epithelium, or even particles of cartilage lying freely in the tissue. All the vestiges are usually found above and dorsal to the hyoid. The branchial apparatus cannot leave remnants in the neck below the hyoid.

5. The thymus originates from the third pharyngeal pouch, in the form of a long canal running obliquely from the lateral pharyngeal wall to the sternum, where the characteristic thymus substance begins to develop.

6. The thymic duct usually disappears either partly or completely. Occasionally, the entire duct or one of its parts may persist.

7. The vestiges of the thymic duct may change into a lateral cervical fistula or cyst. If the entire duct persists, a complete fistula results; when only a part of it, an incomplete one.

8. The anatomic situation of the lateral fistula corresponds very closely with the course of the thymic duct. The walls of the lateral fistulas are generally covered with squamous epithelium, but ciliated epithelium is occasionally found.

9. The lateral thyroid lobes also have a short canal which disappears early. By analogy with the thymic duct one can consider that this canal may also persist and form fistulas and cysts.

The author cites a case of a young girl on whom he operated for lateral cervical fistula by the von Hacker method. The tract was injected with methylene blue and dissected out completely, the upper end opening into the nasopharynx. The result was a complete cure.

MILLER, Chicago.

TELEOROENTGENOGRAPHY AS AN AID IN ORTHOPEDIC MEASUREMENTS. P. M. HICKEY, Am. J. Roentgenol. **11**:232 (March) 1924.

By using a long cassette fitted with two sets of 14 by 17 intensifying screens accurately matched end to end, the author obtained a total film length of 34 inches and a width of 14 inches. With the tube at 7 feet, accurate measurements of the lower limbs were made. It was used to good advantage in measuring the femur and tibia in congenital dislocation of the hip, and in hypoplasia following anterior poliomyelitis and tuberculosis of the hip. Lewin, in the discussion, regards this method very useful in arriving at the amount of bone to be removed in leveling a pelvis of curvature of the spine, with inequality of length of legs.

STULIK, Chicago.

Book Review

LEHRBUCH DER GRENZGEBIETE DER MEDIZIN UND ZAHNHEILKUNDE. With the collaboration of Prof. DR. O. BUETTNER, Rostock i. M.; Prof. DR. G. FINDER, Berlin; Prof. DR. E. FULD, Berlin; Prof. DR. F. GROSSMANN, Berlin; Prof. DR. A. GUTMANN, Berlin; DR. E. HERZFELD, Berlin; Ministerialrat DR. F. KOELSCH, München, Geheim Sanitäts-Rat; DR. H. KRON,* Berlin; DR. R. LEDERMANN, Berlin; DR. J. MISCH, Berlin; DR. H. MUCHSAM, Berlin; DR. G. TUGENDREICH, Berlin. Editor, DR. J. MISCH. 2 Volumes. Third Edition, with 596 partly colored illustrations. Vol. 1, pp. 700. Vol. 2, pp. 682. Leipzig, F. C. W. Vogel, 1923.

By leaving a greater margin on the page, the remarks of the dentist editor, Dr. Misch, are easily recognizable because of his unusual acquaintance with many fields of medicine. This gives a certain uniformity of treatment. It is hardly possible to give more than an idea of the scope of the work. The headings of the main divisions are: "Mouth Digestion, Salivary Glands, Inflammations of Salivary Glands, Inflammations of Mucous Membrane of Mouth." "Disturbances of Development, Internal Secretion." Exogenous intoxications with such substances as are used in dental work. This division contains special chapters on narcotics and the theories of narcosis. "Diseases of Metabolism and Blood." "Infectious Diseases." "Circulatory Diseases." "Stomach Diseases in Their Relation to Diseases of Teeth and Mouth."

The pediatrician will be particularly interested in the chapters dealing with the diseases of children. "Anatomy and Physiology" of the suckling and of the secretions of mouth and saliva are discussed. "Dentition" is given its proper space, and perhaps a little too much significance is attached to its possible dangers. "The Relation of Diseases of Children to Diseases of Teeth and Mouth" includes rachitis, spasmophilic diathesis, tuberculosis, scrofulous and exudative diatheses, hereditary syphilis, scurvy, and acute osteomyelitis. "Acute Infectious Diseases" include chickenpox, measles, german measles, scarlet fever, and diphtheria. "Primary Disease of the Mouth," "Diseases of the Tongue," and "Malformation" form other subdivisions, while some pages are devoted to the care of the mouth in childhood, the sucking of the thumb and other bad habits, as well as to narcosis, general and local, in childhood. The importance of proper care of the milk teeth is strongly emphasized. It is truly remarkable how many dentists do not seem to understand this, not to mention the lack of knowledge on the part of physicians.

The next big subdivision deals with the nervous diseases subdivided into "Disease of Peripheral Nerves," "Organic Disease of Cord and Brain," "Mental Diseases," "Abnormal Condition with Nervous Symptoms," and "Hypnotism and Suggestion."

The fourth large subdivision is devoted to "Syphilitic Diseases," where the pathologic anatomy, subjective complaints and disturbances of function, diagnosis, transmissibility to animals and immunity, prognosis, heredity, prophylaxis of mouth syphilis, distribution and therapy are discussed. This concludes the first volume.

The second volume opens with the "Diseases of the Skin," including the occupational types. The division of "Diseases of Women," including obstetrics, contains many interesting data. In the seventh division, "Diseases of Nose, Throat and Larynx," the influence of mouth breathing on the mandibles and

* Dead.

on occlusion of the teeth is treated at length. These chapters are of the greatest interest to the pediatrician. The eighth big subdivision covers "Diseases of the Ear." The ninth subdivision takes up "Diseases of the Eye," and the tenth deals with "Industrial Diseases." An index closes the second volume.

At times it seems that the purely medical text could be shortened with advantage. The book is of great interest.

News and Comment

There will be as guests of the Pediatric Section at the A. M. A. Convention this year, Dr. Leonard Findlay of Glasgow University, Edinburgh, Scotland, and Professor Heinrich Finkelstein of Berlin. Dr. Findlay is well known for his recent work on "Rickets," and Dr. Finkelstein for his work on "Diseases of Nutrition" and also for a most excellent textbook on "Diseases of Infancy."

The American Pediatric Society will hold its thirty-sixth Annual Meeting on June 5, 6 and 7, at the Maplewood, Pittsfield, Mass. Dr. D. M. Cowie of Ann Arbor, Mich., will preside as President. The program will consist of six sessions with a total of twenty-six papers. This program gives a commendable admixture of both clinical and laboratory papers.

CORRECTION

In the article of Dr. D. C. Mebane, THE AMERICAN JOURNAL OF DISEASES OF CHILDREN, March, 1924, page 219, first paragraph, third line, the phrase "the prevention of mental disease" should read "the prevention of dental disease."